MENTAL HEALTH DISORDERS AND SUBSTANCE USE AMONG ADOLESCENTS AND YOUNG ADULTS

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Abstract

Background: Mental health disorders and substance use contribute significantly to the burden of disease worldwide. These two conditions are relatively common among adolescents and young adults. Mental health disorders and substance use problems are closely linked, and both conditions can share similar biological, psychological, and social components. The co-occurrence of these two conditions presents complex challenges in their prevention, diagnosis, and treatment. If left untreated, these conditions may result in loss of productivity, poor educational outcomes, inefficient use of limited healthcare resources, and a higher prevalence of chronic diseases.

Methods: A systematic review and meta-analysis was conducted to determine and quantify the association and directionality between mental health disorders and substance use among adolescents and/or young adults. Following this, the prevalence and association between mental health disorders and substance use among students attending Canadian post-secondary institutions was determined analyzing the American College Health Association - National College Health Assessment II - Canadian Reference Group survey, spring 2016.

Results: Our systematic review and meta-analysis showed a significant association between depression and use of alcohol, cannabis, and tobacco. Significant associations were found between anxiety and use of alcohol, cannabis, and tobacco. A bidirectional relationship was observed with tobacco use at baseline leading to depression at follow-up and depression at baseline leading to tobacco use at follow-up. A unidirectional relationship was observed with cannabis use leading to depression. Our secondary data analysis showed that the odds of having depression were greater for current and former tobacco users. Current cannabis users with or without other mental health disorders were more likely to have depression. Also, former cannabis users without other mental health disorders were more likely to have depression. The odds of having anxiety were greater for current and former female alcohol users.

Conclusion: The findings and recommendations of this thesis can be used to assist healthcare professionals, health promoters, and policymakers when dealing with mental health disorders and substance use. By affecting change at the personal, interpersonal, and societal levels, we can assist adolescents and young adults to make better choices, seek supports as needed, and live healthier and well-adjusted lives.

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Chapter 1: Introduction

1.1 Mental health and mental health disorders

Mental health refers to “a state of well-being in which every individual realizes his or her own potential, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to his or her community" (1). Mental health is important at every stage of a person’s life. It has a direct influence on children’s and adolescents’ development, young adults’ educational attainment, adults’ work-related productivity and shapes their adult personality and characteristics.

Mental health disorders are defined as any alterations or abnormalities in thought, mood, perception, and/or behavior that can be attributed to distress and impair functioning (2). There are a number of mental health disorders with different presentations from mood and anxiety disorders to psychosis, dementia, intellectual disabilities, and developmental disorders. Mental health disorders are known to be the leading cause of ill-health and disability worldwide (3). It is reported that more than 450 million people across the globe suffer from mental health disorders (3). In Canada, about 9.1 million people are directly affected by a mental health disorder at some point in their lives, and many others are indirectly impacted by way of a family member, friend, or co-worker (4).

Globally, mental health disorders are one of the leading causes of disease burden (3). Based on published data in 2016, mental health disorders account for 32.4% of years lived with disability compared to earlier estimate of 21.2% in 2013 (5). Additionally, a large number of individuals with mental health disorders remain undiagnosed and therefore, untreated, causing a major public health concern (6). It is reported that approximately two-thirds of patients who suffer from mental health disorders (35-50% in developed and 76-85% in developing countries) never seek professional help from a healthcare provider (6). This can be attributed to a variety of reasons

including 1) limited access to mental health treatment and social support services; 2) social stigma frequently associated with mental health disorders and the fear of discrimination which may discourage individuals from seeking and receiving the treatment they need; and 3) insufficient allocation of financial and human resources to help diagnose and treat individuals with mental health disorders.

There are many factors that may contribute to poor mental health, including a) genetic and biological factors (such as chromosomal abnormalities and intelectual disability), b) individual characteristics and behaviors (such as poor emotional and social intelligence, low self-confidence, poor communication skills, and medical illnesses and substance use), c) social circumstances (such as loneliness, family conflicts, exposure to violence or abuse, low income and poverty, difficulties or failure at school, and work related stress), and d) environmental factors (such as poor access to basic medical services, social supports and gender inequalities, and discrimination) (7). Poor mental health can be detrimental to people's overall health and cause a substantial financial burden to our society.

In Canada, the direct neuropsychiatric-related expenses on hospital stay, physician care, and medications are estimated to be $11 billion Canadian dollars (CAD) (8). The majority of expenses go toward mood/anxiety and alcohol/drug use disorders ($5 billion CAD) (8). According to the World Health Organization (WHO), the rate of work absenteeism as a result of mental health disorders represents a bigger problem than the one attributed to poor physical health (9). It is noteworthy to mention that mental and physical health are intricately linked. There is a bidirectional relationship between mental and physical health. For instance, mental illness can be a risk factor for the development of chronic physical ailments, and poor physical health can lead to the development of mental health disorders (10, 11).

The two most common types of mental health disorders are mood and anxiety disorders (12). Globally, depression and anxiety are ranked as the first and sixth most common causes of years lived with disability (YLD) and significantly contribute to the overall poor quality of life (13).

1.1.1 Depressive disorders

Depressive disorders are a group of disorders which include symptoms such as depressed mood or significantly diminished interest or pleasure, weight loss/gain, insomnia/hypersomnia, loss of energy, psychomotor agitation/retardation, feelings of guilt, loss of concentration, or suicidal ideation. Severity may be coded separately and depends on various factors, depending on the specific disorder (14).

Depression is the most common mental health disorder and the leading cause of disability in the world. Globally, more than 300 million people (4.4% of the world's population) are estimated to suffer from depression (13). Depression is more common among females, single or divorced individuals, those who have family history of the disease, experienced traumatic life events, and those with alcohol/drug use disorders (15). According to WHO, the Americas (United States, Mexico, and Canada) is ranked as the geographical region with the fourth highest prevalence for depressive disorders (13). In 2015, it was estimated that 4.7% of Canadians suffered from depressive disorders, which accounted for 6.9% of the total YLD (13).

1.1.2 Anxiety disorders

Anxiety disorders are a group of disorders which include symptoms such as anxiety, excessive worrying and panic attacks, which are serious enough to interfere with a person's functioning (14). Anxiety can be presented by symptoms such as muscle tension and vigilance in preparation for the forthcoming danger. The severity and duration of anxiety symptoms may vary between people and over time. There are many patients who suffer from anxiety symptoms even though they do not meet the criteria for the clinical diagnosis of anxiety disorders. Diagnosis of each anxiety disorder is only made after ruling out the physiological effects of substance or medication and in the absence of better explanation by another mental disorder. The age of onset for many anxiety disorders is in childhood with tendency to persist over time if left untreated. According to DSM-V the list of different anxiety disorders in developmental order are as follow: separation anxiety disorder, selective mutism, specific phobia, social anxiety disorder (social phobia), panic disorder, panic attack specifier, agoraphobia, generalized anxiety disorder (GAD),

substance/medication-induced anxiety disorders and anxiety disorder due to another medical condition (14). Social phobia usually develops during childhood or adolescence, panic disorder typically begins in late adolescence or early adulthood, and GAD can develop at any point in time but most commonly occurs between childhood and middle age (14). The proportion of people living with anxiety disorders in the world is 3.6% (approximately 264 million people) with the third highest rates reported in the region of the Americas (13). Specifically, in Canada, it is estimated that nearly 8.5 million people (20%) are at risk of suffering from an anxiety disorder in their lifetime. In fact, 1.6 million Canadians (4.9%) have been diagnosed with anxiety disorders, which represents 4% of the total YLD (13).

1.2 Substance use and substance use disorders

Substance use is a broad term defined as taking any substance which can eventually lead to alteration of the mental, physical, or emotional functioning of the body. There are different stages of substance use starting from initiation to occasional use and/or eventual addiction, which depend on the interplay of multiple risk factors. These factors can be broadly categorized into a) biological (such as age and sex), individual (such as personality and family history of substance use), b) social (education, employment, and peer pressure) and c) environmental (such as availability and access to substances) components (15). The diagnosis of substance use disorder is based on 11 criteria, including 1) harmful use of substances, 2) social problems related to use, 3) interpersonal problems related to use, 4) spending a lot of time on substance use, 5) withdrawal symptoms, 6) the presence of a tolerance effect, 7) increasing amount or longer duration of substance use, 8) inability to cut down or quit using substances, 9) craving for substances, 10) physical/psychological dependance/problems related to use, and 11) foregoing major activities (such as home, work, or school activities) because of substance use. A patient must have at least two criteria within a 12-month period to be diagnosed with a substance use disorder (16).

Substance use disorders account for a considerable share of the global burden of disease including disability and premature loss of life (17). Globally, it is estimated that 250 million people are substance users (18). In Canada, 2.1% of the population (2.8% males and 1.5%

females) suffer from substance use disorders (19). Alcohol, cannabis, and tobacco are reported to be the three most commonly used substances, worldwide. The global prevalence of alcohol use (heavy episodic drinking within the past 30 days), tobacco smoking (daily), and cannabis use (within the past year) were estimated at 16%, 15%, and 3.8%, respectively (18-20). In 2015, Canada reported a prevalence of alcohol use (heavy episodic drinking) at 15% (4.2 million people), tobacco smoking (daily) at 9% (2.8 million people), and cannabis use (within the past year) at 12% (3.6 million people) (21). Although tobacco and alcohol use are known to cause high rates of morbidity and mortality, not enough is known about the effects of cannabis use in our society. This issue becomes increasingly important when one considers an increasing trend in prevalence of cannabis use in Canada (22) and the fact that cannabis will be legal as of October 17, 2018 (23).

1.2.1 Tobacco

Tobacco is one of the most commonly used addictive substances and the leading cause of premature mortality in Canada and the world (24, 25). Tobacco is highly addictive, and its long-term use can lead to nicotine dependence and consequently, withdrawal symptoms for those who wish to quit (24, 25). It is widely known that tobacco use can cause a number of serious physical ailments, but there is less awareness about its detrimental effects on mental health. Early age of initiation is critically important with nearly 51.4% of tobacco users starting to smoke before the age of 18 years old (26). There are different factors associated with the early initiation of tobacco use, which include: a) environmental influences (such as social norms associated with peer and parental smoking behaviors and mass media advertising through the use of popular movies and music videos), b) biological (such as age and sex) and c) personality traits (such as rebelliousness and sensation-seeking) (27). Other risk factors that may be related to the initiation of tobacco use at a young age include: a) low socioeconomic status, b) availability, c) accessibility, and affordability of tobacco products, d) the presence of stress, e) low self-esteem, f) low level of academic achievement, and g) mental health disorders (27).

1.2.2 Alcohol

Alcohol is known as a psychoactive substance which can cause dependency. Alcohol use can have a negative impact on an individual's health, poses a risk to others and places a significant financial burden on our society (28). Globally, alcohol is known as the third leading risk factor for premature death and disability (29). Alcohol use is a risk factor for many chronic conditions (such as certain cancers, psychiatric disorders, cardiovascular and gastrointestinal diseases) (30). In 2012, alcohol use contributed to 3.3 million deaths (5.9%), globally (20). According to the Canadian center on substance abuse, most of the substance use related hospitalizations in Canada were due to alcohol use (31). Alcohol use is associated with an increased risk for alcohol use disorders, sexual assaults, and even serious death including those caused by car accidents (15, 32). Driving under the influence of alcohol was recognized as the leading cause of criminal death in Canada in 2008 (33).

1.2.3 Cannabis

Cannabis is the most commonly abused illicit drug worldwide (34). The prevalence of cannabis use is estimated to be 2.5% (147 million people), globally (35). The most rapid growth in cannabis use is reported to take place in developed countries, including those in North America, Western Europe and Oceania (35). It is reported that the median age of cannabis initiation was 17 years old in Canada (21). Cannabis use has both acute and chronic adverse health effects on its users. Acute effects of cannabis use may include cognitive impairment and interruption in psychomotor performance (which may increase the risk for a motor vehicle accident) (35). Chronic effects include respiratory damage (such as bronchitis, persistent lung inflammation, epithelial injury of the trachea) and exacerbation of certain mental health disorders (such as psychosis and schizophrenia) (35). There is growing concern that legalization of cannabis in many countries including Australia, Netherlands, parts of the United States and most recently Canada, may lead people to develop a false perception that it is safe to use and subsequenlty, underestimate the serious nature of the health hazards posed by cannabis (36).

1.3 Adolescents and young adults

Adolescence (ages 10-17 years old) and young adulthood (ages 18-24 years old) are developmental periods markedly known for physical, mental, and emotional changes and growth. This age group (ages 10-24 years old) constitute about one fifth (18%) of Canada's population in 2017 (37). Attention to the health, particularly mental health, of this age group is often neglected as they are thought to be the healthiest subgroup within the general population. The mental health status of adolescents and young adults has a direct influence on their social contributions, productivity, education, employment, physical health, and overall well-being. Adolescents' and young adults' development and growth can be disrupted by a variety of physical or mental health illnesses. Mental health and substance use problems are two conditions that are more likely to be reported during adolescence and young adulthood (38).

Worldwide, the prevalence of mental health disorders among adolescents and young adults is 10-20% (39). Mental health disorders are the leading cause of disability among this vulnerable population, accounting for 45% of total morbidity (40). Depression and anxiety are the two most common mental health disorders affecting young people (12). In Canada, about 11% of individuals aged 15 to 24 years old have experienced at least one episode of major depressive disorder (41). In 2009, the prevalence of anxiety disorders was 4% among Canadians aged 12 to 19 years old and 5.8% among those aged 20 to 29 years old (42).

The diagnosis of mental health disorders among young people is challenging as it may be confused with the typical mood swings related to the transition from childhood to young adulthood. Prevention is better than treatment when it comes to the management of mental health disorders among adolescents and young adults. Management of mental health disorders should be in line with the need to address underlying causes such as school and work related stress, peer pressure, and identifying possible concomitant disorders.

Substance use is another major health issue facing this age group (10-24 years old). Self-identity and a higher tendency for exploration and risk-taking are characteristics of young adults. These factors combined with social pressure from peers and the wider influence of social media may

encourage adolescents and young adults to use substances. Adolescents are at increased risk of transitioning from experimental substance use to substance use disorders as their brain and body are still in the developmental stage (43). Substance use may alter the mental, physical, or emotional function of the body, reduce self-control and increase risky behaviors and violence (44, 45). It is reported that the likelihood of developing a substance use disorder among those who initiated use of an addictive substance by the age of 14 years old was greater than those who start after the age of 21 years old (46). In Canada, the prevalence of substance use disorders is nearly 3.6% among Canadians aged 15-19 years old and 5.6% among those age 20-24 years old (19).

1.3.1 Students

Issues related to poor mental health and substance use are a growing public health concern among university aged students. In 2016, 14.7% of Canadian post-secondary students reported that they have been diagnosed or treated for depression and 18.4% for anxiety within the past 12-months. (47). School-related challenges such as coursework and examination stress, financial difficulties and separation from family and childhood friends may consider factors related to mental health problems for this age group. It is reported that number of students seeking mental health services and presenting with more severe psychological issues have risen significantly in Canadian post-secondary campuses (48). A study conducted among Ontario's college students showed that students with poor mental health had challenges (such as alertness/attention challenges and memory/executive function problems) with their academic performance (49). Another serious problem facing students is substance use. Evidence suggests that prevalence of alcohol, cannabis, and tobacco use is high among Canadian post-secondary students (47). Engaging in such behaviors may be related to the stress associated with the academic environment, competition with other students, peer influence, and the need for social acceptability and belonging.

1.4 Relevance

Substance use and mental health disorders are two conditions that significantly affect the mood, thinking, and behavior of an individual. There are reports of high prevalence of substance use and mental health disorders among adolescents and young adults in Canada (12, 21). According to a

study, people with mental health disorders were two times more likely to have a substance use problem compared to the general population and people with substance use problems were nearly three times more likely to have a mental health disorder (50). Dealing with substance use or mental health disorders is quite difficult, and it becomes even more challenging when there is a co-occurrence of both conditions among young people. Openly and proactively addressing adolescents' and young adults' mental health needs and substance use related problems can have a positive impact on an individuals' academic, personal, and professional life, and that of their families, and communities. One of the hypotheses used to help explain the dual co-occurrence of substance use and mental health disorders is the self-medication hypothesis (51). It is postulated that people use a substance as a potential therapy to medicate the uncomfortable effects of mental health symptoms (51). For instance, a depressed person may use cannabis to relieve his/her symptoms of sadness and/or an anxious person may use alcohol to feel more relaxed in social settings. Given the high prevalence of mental health disorders and substance use, it is important that patients diagnosed with mental health disorder and/or a substance use be evaluated and if need be, treated for both conditions.

The findings and key recommendations of this thesis can be used to assist healthcare professionals, health promoters, and policymakers when dealing with mental health disorders and substance use among adolescents and young adults. It can also provide them with critical insight when planning initiatives aimed at reducing the burden of depression and anxiety among adolescents and young adults with a focus on substance use. This will permit more effective and efficient use of their limited financial and human resources.

1.5 Objectives

1. To determine and quantify the association and directionality between mental health disorders and substance use among adolescents and/or young adults by conducting a systematic review and meta-analysis.
2. To determine the prevalence and association between mental health disorders and substance use among students attending Canadian post-secondary institutions by analyzing the

American College Health Association - National College Health Assessment II (ACHA-NCHA II) - Canadian Reference Group survey, spring 2016.

1.6 Methods

To address the first objective of our study a systematic review and meta-analysis was conducted. The research question was developed describing the Populations of interest (adolescents and young adults), Exposures (Substance use, such as alcohol, cannabis, and tobacco), Comparators (adolescents and young adults not using substances), and Outcomes (anxiety and/or depression) (PECO). The PECO statement was the foundation of the entire systematic review upon which the search strategy, inclusion/exclusion criteria, data extraction, and synthesis of results was based. Once the research question was defined, an appropriate protocol for the systematic review and meta-analysis was developed. The literature search used relevant databases and snowballing techniques. Dual independent title, abstract, and full-text screening of all eligible studies were conducted based on the inclusion/exclusion criteria. Data were extracted, the methodological quality of included studies was assessed, and results were summarized. Meta-analysis was used to quantify the pooled results from the included studies. Finally, publication bias and sub-group analysis was assessed (refer to chapter two).

To address the second objective, multiple logistic regression was conducted. The ACHA-NCHA II - Canadian Reference Group survey, spring 2016 was the source of data for this study. Initial descriptive statistics were reported for the dependent (depression/anxiety) and independent (alcohol, cannabis, and tobacco) variables of interest. Unconditional analysis was conducted to estimate the relationship between the exposures of interest (substance use) and outcomes (mental health disorders). The independence of the exposure variables, accounting for potential confounders, and interaction terms were evaluated while building the models. Two separate multiple logistic regression models were built for predictive modeling (refer to chapter three).

1.7 Summary

Mental health disorders and substance use contribute significantly to the burden of disease worldwide. The co-occurrence of these two conditions, especially among adolescents and young adults is a serious public health concern. Oftentimes, mental health disorders and substance use are underdiagnosed and remain unidentified. This is troubling due to the plethora of associated sequelae negatively impacting health, academic, personal, and professional life. This thesis aimed to comprehensively explore the association and directionality between mental health disorders and substance use in peer-reviewed studies and to identify the prevalence and association between these two conditions among Canadian post-secondary students. Findings of this thesis provide valuable insights and recommendations to healthcare professionals, policymakers and health promoters to better address challenges related to mental health disorders and substance use.

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Chapter 2: Examining the association and directionality between mental health disorders and substance use among adolescents and young adults in the U.S. and Canada – A systematic review and meta-analysis

2.1 Abstract

Background: Mental health disorders and substance use contribute significantly to the burden of disease worldwide. Among adolescents and young adults, mental health disorders play an important role and place them at an increased risk for academic failure, criminal activity, and substance use. Substance use is a concern among this age group and negatively impacts their physical health and psychosocial development. The purpose of this systematic review was to examine the association and directionality between mental health disorders and substance use among adolescents and young adults in the U.S. and Canada.

Methods: The following databases were used: Medline, PubMed, Embase, PsycINFO, and Cochrane Library. Dual title and abstracts were reviewed followed by full-text screening. Meta-analysis used odds ratios as the pooled measure of effect. Where possible, causal relationships and the direction of causality was assessed using longitudinal studies.

Results: After screening, 36 out of 3,656 studies were selected. Pooled results of the meta-analysis showed a positive association between depression and use of alcohol (OR=1.50, 95% CI: 1.24-1.83), cannabis (OR=1.29, 95% CI: 1.10-1.51), and tobacco (OR=1.65, 95% CI: 1.43-1.92). Significant associations were found between anxiety and use of alcohol (OR=1.54, 95% CI: 1.19-2.00), cannabis (OR=1.36, 95% CI: 1.02-1.81), and tobacco (OR=2.21, 95% CI: 1.54-3.17). A bidirectional relationship was observed with tobacco use at baseline leading to depression at

follow-up (OR=1.87, CI=1.23-2.85) and depression at baseline leading to tobacco use at follow-up (OR=1.22, CI=1.09-1.37). A unidirectional relationship was also observed with cannabis use leading to depression (OR=1.33, CI=1.19-1.49).

Conclusion: This study offers insights into the association and directionality between mental health disorders and substance use among adolescents and young adults. The results of this study can help guide key stakeholders in making recommendations for interventions, policy and programming. Having up-to-date information about the relationships between mental health disorders and substance use is critical for professionals working with this vulnerable population to more effectively tailor services to comprehensively treat both of these conditions.

Keywords: Depression, anxiety, alcohol, cannabis, tobacco, adolescents, young adults

2.2 Introduction

Mental health disorders and substance use are important problems and relatively common among adolescents and young adults (1). These two conditions are the leading cause of years lived with disability worldwide (2). People are more likely to initiate substance use during adolescence, a critical period in one's life as they transition from childhood to adulthood (3). It is estimated that 50% of all mental health disorders start by the age of 14 years old and 75% by the age of 25 years old (4). Mental health disorders and substance use problems are closely linked, and both conditions can share similar biological and environmental components (5, 6).

Mental health disorders contribute significantly to the burden of disease (2). Globally, approximately one in five adolescents experience a mental health disorder each year (7). Depressive and anxiety disorders are quite prevalent among adolescents and young adults. In the U.S., 8.4% of adolescents were diagnosed with either anxiety or depression in their lifetime (8). In Canada, 5% of adolescents were diagnosed with an anxiety disorder and 6.3% with a mood disorder, mainly depression (9). Despite the magnitude of the problem posed by mental health disorders among adolescents and young adults in the U.S. and Canada, frequently they are undiagnosed and when diagnosed not treated properly (10).

Adolescents and young adults with mental health disorders are at an increased risk for many negative health and social outcomes including self-harm and suicide (11), poor academic performance (12), and involvement in risky behaviors and poor sexual health (13). Risk factors for mental health disorders include biological factors (such as genetic tendency, head trauma, and substance abuse), psychological factors (such as maladaptive personality traits, difficult temperament, and physical/sexual abuse), and social factors (such as family conflict, loss of a loved one, bullying, and academic failure) (14).

Substance use among adolescents and young adults is a growing public health concern in developed countries such as the U.S. and Canada. Alcohol, cannabis, and tobacco are the substances most commonly used by adolescents and young adults. In Canada, the highest prevalence of alcohol (83%), cannabis (30%), and tobacco (18%) use was seen among young adults aged 20 to 24 years old followed by adolescents aged 15 to 19 years old (alcohol: 59%, cannabis: 21%, and tobacco: 10%) (15). Similar trends in the prevalence of substance use were seen in the U.S. (16). The magnitude of substance use among adolescents and young adults represents a major public health concern.

Substance use among adolescents and young adults is associated with many negative health, social, and economic consequences. These vary from suicidal behaviors (17) to low academic performance and school dropout (18), employment problems later in life (19), and risky behaviors (20). Moreover, initiation of substance use in adolescence may be associated with the development of substance abuse and substance dependence later in life (21). Risk factors associated with substance use are found at the individual (such as age, sex, personality and family history of substance use), interpersonal (such as relationship with parents, siblings, and peer pressure), and environmental (such as social norms, availability and accessibility of substance) levels (22).

Evidence suggests a complex interplay between substance use and vulnerability to mental health disorders. Several hypotheses have been postulated regarding the co-occurrence of these two conditions. The self-medication hypothesis suggests that coping with psychological pressures and stressors as they relate to maturation, untreated traumas, and underlying conditions may lead to

substance use and related risky behaviours (23). Moreover, environmental, genetic, and personality factors may predispose an individual to develop substance use problems and mental health disorders (22). However, it is less clearly established whether substance use and/or mental health disorders by themselves can lead to the development of either condition.

Previous studies have been conducted examining the relationship between mental health disorders and substance use. Some studies have suggested that an association exists between depression and/or anxiety and alcohol, cannabis or tobacco use (24-29). However, findings in the literature have been inconsistent (30-35). Due to the high prevalence of mental health disorders and substance use among adolescents and young adults and the high potential of co-occurrence, further research in this important area is warranted. The purpose of this study was to examine the association and directionality between the three most common substances used (alcohol, cannabis, and tobacco) and two mental health disorders (depression and anxiety) among adolescents and young adults in the U.S. and Canada.

2.3 Methods

2.3.1 Data sources

We conducted an extensive systematic literature review on the following electronic databases: Medline, PubMed, Cochrane Library, Embase, and PsycINFO. Our searches consisted of two major categories and their corresponding MeSH terms and keywords: 1) Substance use behaviors: alcohol drinking, alcohol use, cannabis, marijuana smoking, marijuana use, smoking, tobacco smoking, tobacco use and 2) Mental health disorders: depression, depressive disorders, major depressive disorder, anxiety, anxiety disorders, and mood disorders. Snowball method (reference tracking) was also used to scan the reference lists of retrieved full-text articles and then to search manually for additional relevant literature.

2.3.2 Data extraction and analysis

Two screeners (SE and NMKS), independently, reviewed the list of identified articles to assess eligibility for inclusion in our study. Any disagreements were resolved by a tiebreaker vote (YB). Extraction criteria included: year of publication, study design, sample size, target population, country where the study was conducted, measurement instrument used for substance use and mental health disorders, effect measure, covariates, and results. The effect measures examined the association between any of the following categories: 1) depression and alcohol use; 2) depression and cannabis use; 3) depression and tobacco use; 4) anxiety and alcohol use; 5) anxiety and cannabis use, and 6) anxiety and tobacco use. If a study discussed more than one of these categories, we extracted and analyzed all relevant effect measures separately.

2.3.3 Definitions of mental health disorders and substance use

The definitions and measurements of mental health disorders and substance use in different studies were heterogeneous. When multiple measures were used, we selected the most standardized and commonly used measure to maximize comparability between studies (Table 2.1) (24-59).

2.3.4 Quality assessment

The modified Newcastle-Ottawa Scale (NOS) was used to assess the quality of both cross-sectional and longitudinal study designs. This scale includes three components: 1) selection of study groups; 2) comparability of the groups; and the 3) ascertainment of the outcomes of interest (60). The quality of each study was determined by assigning them to one of three subgroups and designated as low, moderate, or high risk of bias.

2.3.5 Meta-analysis

Statistical analysis was completed using the Comprehensive Meta-Analysis software version 3 (Biostat Inc., New Jersey, USA). For pooled mean effect size, random-effects models were used

because differences were expected in the methodology and the samples of selected studies (61). The primary outcome measure was Odds Ratio (OR). ORs and 95% confidence intervals (CI) were either extracted from the articles or calculated by the authors using the quantitative data provided in the studies. Six separate meta-analyses were conducted (Table 2.2). Q-statistics and I^2 were used to examine the heterogeneity among studies. Publication bias was assessed by graphing funnel plots to visualize any possible asymmetries and Duval and Tweedie's trim and fill test was conducted to adjust the results in case of publication bias (62). Sensitivity analysis was done using one-study removed analysis. Moreover, subgroup analysis was performed using moderator variables including point estimate (crude or adjusted), target population (adolescents and young adults), severity of mental health disorders (symptoms and disorders), and intensity of substance use behavior (definitions).

2.4 Results

2.4.1 Study selection and characteristics

In total, 3,656 articles were identified by the initial search. After removing studies prior to the year 2000 and duplicates, 2,341articles remained. Title and abstract screening excluded 2,177 articles, leaving 164 for full-text screening. After the full-text screening, 30 articles remained. Six additional articles were manually added by use of the snowball method. All 36 selected articles used either a cross-sectional (n=19) or longitudinal (n=17) study design. The summary of our study selection is shown in a PRISMA diagram (Figure 2.1). Study characteristics are presented in Table 2.2. The quality of studies was assessed using a modified Newcastle-Ottawa scale (NOS), which found 5 studies with a low, 27 with a moderate, and 4 with a high risk of bias.

2.4.2 Synthesis of results

The results of the meta-analysis found significant positive associations between depression and alcohol use (OR=1.50, 95% CI: 1.24-1.83), cannabis use (OR=1.29, 95% CI: 1.10-1.51) and tobacco use (OR=1.65, 95% CI: 1.43-1.92). Similarly, significant positive associations were

found between anxiety and alcohol use (OR=1.54, 95% CI: 1.19-2.00), cannabis use (OR=1.36, 95% CI: 1.02-1.81) and tobacco use (OR=2.21, 95% CI: 1.54-3.17) (Table 2.3).

2.4.3 Analysis of the directionality

The directionality of the association between each relevant category was assessed by pooled analysis of the longitudinal studies. Results showed that there was a significant positive bi-directional association between tobacco use at baseline leading to depression at follow-up (OR=1.87, CI=1.23-2.85) and depression at baseline leading to tobacco use at follow-up (OR=1.22, CI=1.09-1.37). Cannabis use at baseline was significantly associated with depression at follow-up (OR=1.33, CI=1.19-1.49) (Figure 2.2).

2.4.4 Subgroup analysis

Due to the heterogeneity detected upon pooled analysis, subgroup analysis was conducted to examine whether the differences within categories could be attributed to specific moderators (age group, measures of mental health disorder, and severity of substance use). Results of our subgroup analysis are summarized in Table 2.4. Results from the subgroup analysis by age group including adolescents (aged 10 to 18 years old) and young adults (aged 18 to 24 years old) found that the association between mental health disorders and substance use remained significant among adolescents but not among young adults. Subgroup analysis based on severity of mental health disorders showed a consistently higher point estimate for clinically diagnosed mental health disorder patients. Finally, subgroup analysis based on the intensity of substance use showed a recurring theme, whereby, as severity increased mental health disorders also increased (Table 2.4).

2.4.5 Publication bias

Funnel plots showed no evidence of publication bias in the included studies which examined the association between depression and alcohol use; depression and cannabis use; depression and tobacco use; anxiety and alcohol use; and anxiety and tobacco use. However, there was evidence of publication bias in the included studies which examined the association between anxiety and

cannabis use. Therefore, in these instances, a Duval and Tweedie's trim and fill method was used to test and adjust for the publication bias in our meta-analysis.

2.5 Discussion

This study was conducted to examine the inter-association and directionality between the two most common mental health disorders (depression and anxiety) and three substances used (alcohol, cannabis, and tobacco) among adolescents and young adults in the U.S. and Canada. Our findings suggest that a significant association exists between depression and the use of alcohol, cannabis, and tobacco. Similarly, significant associations were found to exist between anxiety and the use of alcohol, cannabis, and tobacco. A bidirectional relationship was observed between depression and the use of tobacco. Additionally, we found evidence that cannabis use at baseline led to depression at follow-up. The results of our study were consistent with those reported in previous systematic reviews (63-65) and provide additional evidence in support of the inter-association between mental health disorders and substance use.

Harmful alcohol use, which has been defined as heavy episodic or binge drinking is an important health issue among adolescents and young adults in the U.S. (66). The adolescent/young adult brain is still developing, and there is evidence to suggest that frequent use of alcohol at this age may lead to mental health disorders including depression (67, 68). Our results support these findings. We found that alcohol use was a significant predictor of higher levels of depression among adolescents and young adults. However, further research is needed in this area with more longitudinal studies, using longer follow-up periods.

A systematic review conducted by Lev-Ran et al. found a positive association between cannabis use at baseline and the development of depression (69). Our results corroborate these findings and demonstrate that the overall pooled estimate for depression among heavy cannabis users was higher, compared to light users. Another systematic review by Number-Kedzior et al. found a significant positive association between cannabis use at baseline and anxiety at follow-up (65). In our study, it was not possible to infer whether such a causal relationship exists due to the lack of sufficient studies on this topic, which fit our inclusion criteria. Proposed mechanisms for the association between cannabis and depression could be due to biological effects from the

alteration in neurotransmitters such as serotonin in the brain (70) and its impact on developing depression and mediating psychosocial factors such as unemployment and educational failure (49). We observed that when adjusting for personal income and years of education, the association between cannabis use and depression was reduced (49).

In our study, we found a stronger pooled estimate for tobacco use predicting depression, compared to depression predicting tobacco use. Moreover, a stronger pooled estimate was observed in those studies that used a clinical measure of depression rather than depressive symptoms. Our results are biologically plausible as there is evidence to suggest that dysregulation in the hypothalamic-pituitary-adrenal axis following smoking interferes with biological and psychological responses and leads to an imbalance in the levels of cortisol. Cortisol is also known as the stress hormone, and it affects mood, and therefore, its imbalance may lead to depression (71). The association between anxiety and tobacco use might be explained by the negative effect of tobacco use on different brain pathways such as neurotransmitter systems, inflammation and the immune system, oxidative and nitrosative stress pathways, neurotrophins and neurogenesis regulations, mitochondrial function, and epigenetic influences. Alteration in abovementioned pathways can also play a role in development of anxiety disorders (72).

2.6 Strengths and limitations

Our study has several strengths. There is a high level of congruence between our findings and those reported in the existing literature. However, this systematic review is unique because 1) it incorporates only studies originating in the U.S. and Canada, 2) it focuses on the adolescent and young adult population, and 3) it examines the associations and directionality between depression or anxiety and alcohol, cannabis, or tobacco use, separately.

Despite its strengths, our study also has some limitations. We found that certain factors such as the study design (longitudinal vs. cross-sectional), the intensity of substance use (light vs. heavy), and the variation in clinical diagnosis (depressive and anxiety disorders vs. symptoms) affect the outcomes of our study. Participant's age (adolescents vs. young adults) also influenced the inter-association between substance use behaviors and mental health disorders. In our review, several

of our included studies used different instruments to measure depression and anxiety and a broad spectrum of measurements for substance use, making results difficult to compare due to their heterogeneity. When extracting data, we were unable to calculate the unadjusted odds ratio from all included studies. Different studies varied in the degree to which they controlled for potential confounders. Variation in the population sampled, length of follow-up in longitudinal studies, and different sample sizes also added to the variability.

2.7 Conclusion

This study offers significant insight into the association and directionality between substance use (alcohol, cannabis, and tobacco) and mental health disorders (depression and anxiety) among adolescents and young adults in the U.S. and Canada. The results of this study can help guide key stakeholders (school administrators, nurses, physicians, public health professionals, and policymakers) in making evidence-based recommendations for school-based interventions, policy, and programming. It is increasingly evident that adolescents and young adults with substance use issues may also suffer from co-occurring mental health disorders. However, they are frequently undiagnosed and consequently, they do not receive the specialized cross-treatment needed to address both conditions. To be most effective, school-based substance use and mental health programmes should consider integrating and expanding their services for patients with dual disorders. Further research is needed to help guide evidence-based treatment and initiatives for this vulnerable population.

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Table 2.1: Definitions of mental health disorders and substance use

Depression
The center for epidemiologic studies depression scale (CES-D) (26, 32, 36-44)
Beck depression inventory-II (BDI-II) (31)
One item question: Whether respondents felt so sad or hopeless almost daily for two consecutive weeks that usual activities were interrupted (24)
Youth self report checklist (8 self-reported symptoms of depression within the past 6 months): I feel guilty, I cry a lot, I deliberately try to hurt myself, I think of killing myself, I feel lonely, I am unhappy, I feel that no one loves me, and I feel worthless (YSR) (45)
A five-item question: within the past 12 months how often have you felt too tired to do things? Felt unhappy, sad, or depressed? Felt hopeless about the future? Felt nervous or tense? And worried too much about things? (46)
Modified version of the children depression inventory (CDI) (47)
Depression medication prescribed by a doctor or a nurse in the last 12 months (27)
National institute of mental health diagnostic interview schedule for children version IV (NIMH-DISC, version IV): A structured diagnostic interview administered by lay interviewers to assess diagnostic criteria for mental disorders in children and adolescents, in accordance with the diagnostic and statistical manual of mental disorders, fourth edition (DSM-IV) (48)
CIDI-SF: 12-month prevalence of major depressive disorder (MDD), based on the Composite International Diagnostic Interview-Short Form (49, 50)
The university of Michigan composite international diagnostic interview (CIDI): A highly structured research diagnostic instrument developed for use by trained lay interviewers to assess the most common diagnoses among children, adolescents, and young adults as described in the DSM-III-R (51, 52)
A 6-item question: During the past 3-month how often you have felt too tired to do things; had trouble going to sleep or staying asleep; felt unhappy, sad or depressed; felt hopeless about the future; felt nervous or tense; worried too much about things (53)
Major depressive episode diagnosis: self-reported depression diagnosed by a medical professional with the past year (25)
The short form (36) health survey (SF-36) (54)
Mental health component of national health and nutrition examination survey (NHANES), assess diagnostic criteria for mental disorders in children and adolescents, in accordance with the diagnostic and statistical manual of mental disorders, third edition (DSM-III) (30, 55)
Anxiety
Social interaction anxiety scale (SIAS) (28, 29, 56, 57)
Diagnostic interview schedule for children, version IV (DISC-IV) (25, 34, 58)
Primary care evaluation of mental disorders (PRIME-MD) (35)
Schedule for affective disorders and schizophrenia for school-age children (K-SADS) (33, 59)
Anxiety medication prescribed by a doctor or a nurse in the last 12 months (27)
National Institute of Mental Health Diagnostic Interview for children (NIMHD) (48)
Alcohol

Ever drinkers: Drinking at least once within a lifetime (51)
Light drinkers: Consuming less than three drinks per week (30)
Moderate drinkers: Drinking without engaging in heavy episodic or binge drinking in the past two weeks (54)
Moderate drinkers: Drinking no more than 1 to 2 drinks per occasion in the past year, and no intoxication or heavy drinking in the past year (25, 43)
Moderate to heavy drinkers: Consuming more than 3 drinks per week (30)
Regular drinkers: Drink at least once a month or more frequently and consume at least three to four drinks when drinking (47)
Current drinkers: Drinking at least one time during the past 30 days (32)
Daily drinking questionnaire (DDQ): The total number of standard alcoholic drinks consumed during the past week by summing the number of drinks reported for each day (28)
Frequent/heavy drinkers: Those who over the past 6 months had a drink at least once a week or had been drunk at least once (58)
Binge drinkers: Men/women as drinking five/four or more drinks per drinking occasion at least once in the past two weeks (25, 31, 32, 43, 50, 54, 56)
Alcohol use disorders identification test (AUDIT) (28, 57)
Diagnostic interview schedule for children, version IV, alcohol use disorder (DISC-IV, AUD) (34)
Primary care evaluation for mental disorders, alcohol use disorder (PRIME-MD, AUD) (35)
Longitudinal interval follow-up evaluation and structured clinical interview for DSM-IV, non-patient version, alcohol use disorder (LIFE and SCID-I/NP, AUD) (59)
Cannabis
Ever cannabis users: Using cannabis at least once within a lifetime (44, 51)
Any use of cannabis or hashish in the past six months (49)
Infrequent cannabis users: Using cannabis at least once per year but not more than once per month (55)
Infrequent cannabis users: Less than weekly cannabis use (29)
Frequent cannabis users: Weekly or more cannabis use (29)
Current cannabis users: Cannabis use at least one time during the past 30 days (26, 31, 32, 39)
The substance abuse module of the composite international diagnostic interview, cannabis use disorder (CIDI-SAM, CUD) (34, 35, 52, 55, 59)
Tobacco
Ever smokers: Smoking at least once within a lifetime (33, 36, 37, 38, 51)
Current smokers: Smoking at least one time during the past 30 days (24, 30, 31, 32, 39, 40, 41, 42, 45, 46)
Regular smokers: Smoking several cigarettes or more per week (47)
Regular smokers: Self-report measure: I'm a regular smoker/I'm a heavy smoker (27)
Daily smokers: Daily consumption of cigarettes or cigars for a continuous 30-day period or longer (27, 33, 49, 50, 58)

Table 2.2: Study characteristics of final references

First author's name, year, country	Sample size	Target population	Substance use measure	Mental health disorders assessment	Controlled variables	OR (95% CI)
Association between Depression and Alcohol use						
Cross-Sectional Studies						
Elissa Weitzman, 2004, U.S. (54)	27687	College students aged 18-24	Binge/ non-drinkers	The 5-item subscale of SF36	Age, sex, ethnicity	Adjusted: 1.05 (0.96-1.14)
Martha Kubik, 2005, U.S. (32)	3466	Grade 7 students	Heavy/ non-drinkers	CES-D, cut-off point of 16.	Age, ethnicity, SES, smoking, cannabis, and inhalants use	Adjusted: 2.03 (1.30-3.17)
Susan Roberts, 2009, U.S. (31)	418	College students	Binge/ non-drinkers	BDI-II, cut-off point of 20	-	Crude: 0.99 (0.61-1.58)
Elisabeth Simantov, 2000, U.S. (47)	5513	Grade 7-12 students	Regular/ non-drinkers	Modified version of CDI, cut-off point of 9	-	Crude: 2.08 (1.79-2.42)
Linda Richter, 2015, U.S. (25)	24445	Adolescents aged 12-20	Binge/ non-drinkers	Diagnosed depression (self-reported)	Sex, ethnicity, and age	Adjusted: 1.45 (1.11-1.91)
Eleanor Hanna, 2001, U.S. (30)	719	Adolescents aged 12-16	Moderate/ non-drinkers	Diagnostic interview schedule, DSM-III	Age, sex, ethnicity, family poverty level, school problem, smoking status	Adjusted: 3.31 (1.39-7.90)
Longitudinal studies: Alcohol use (exposure) → Depression (outcome)						
Mallie Paschall, 2005, U.S. (43)	13892	Grade 6-12 students	Moderate/ non-drinkers	CES-D, cut-off point of 16.	-	Crude: 1.17 (1.11-1.23)

David Brook, 2002, U.S. (51)	736	Adolescents aged 14, 13-year follow-up	Ever/ never users	Modified version of CIDI	Age, sex, parental educational level, family income, prior psychiatric disorders	Adjusted: 1.72 (1.35-2.20)
Longitudinal study: Depression (exposure) → Alcohol use (outcome)						
Kiyuri Naicker, 2012, Canada (50)	681	Adolescents aged 16-17, 10-year follow-up	Heavy/ non-drinkers	CIDI-SF, cut-off point of 5	Sex and SES	Adjusted: 1.78 (1.10-2.88)

Association between Depression and Cannabis use						
Cross-Sectional Studies						
Lee Ridner, 2005, U.S. (39)	895	College students aged 18-24	Current/ non-users	CES-D, cut-off point of 16	-	Crude: 1.27 (1.00-1.61)
Susan Roberts, 2009, U.S. (31)	418	College students	Current/ non-users	BDI-II, cut-off point of 20	-	Crude: 1.99 (1.23-3.22)
Martha Kubik, 2005, U.S. (32)	3466	Grade 7 students	Current/ non-users	CES-D, cut-off point of 16	Age, ethnicity, SES, smoking, alcohol, and inhalants use.	Adjusted: 1.02 (0.66-1.57)
Longitudinal studies: Cannabis use (exposure) → Depression (outcome)						
Daniel Rasic, 2012, Canada (26)	976	Grade 10 students, 2-year follow-up	Current/ non-users	CES-D, cut-off point of 22 (M) and 24 (F)	Sex	Adjusted: 1.24 (1.05-1.46)
Katholiki Georgiades, 2007, Canada (49)	1282	Adolescents aged 12-16, 14-year follow-up	Past 6-month/non-users	CIDI-SF	Physical health, life satisfaction, personal income, years of education	Adjusted: 1.97 (0.81-4.81)

David Brook, 2002, U.S. (51)	736	Adolescents aged 14, 10-year follow-up	Ever/ never users	Modified version of CIDI	Age, sex, parental educational level, family income, prior psychiatric disorders	Adjusted: 1.36 (1.14-1.62)
Naomi Marmorstein, 2011, U.S. (55)	1252	Adolescents aged 17, A 6-year follow-up	CUD/ non-users	The structured clinical interview for DSM-III-R.	MDD by age 17 and gender	Adjusted: 1.86 (1.11-3.11),
Valerie Harder, 2008, U.S. (52)	1494	Adolescents aged 12-16, 7-year follow-up	CUD/ non-users	CIDI, DSM IV diagnostic criteria for major depression.	Ethnicity, family income, free lunch, tobacco, alcohol, and other illegal drug use, parental monitoring, concentration, behavior problems, shyness, anxiety symptoms, intervention status	Adjusted: 1.33 (0.70-2.53)
Longitudinal study: Depression (exposure) → Cannabis use (outcome)						
Cynthia Suerken, 2014, U.S. (44)	3146	College students, A 6-month follow-up	Ever/ never users	CES-D, Iowa short form	Sex, ethnicity, parental education and spending money available, varsity athlete, club, intramural sports, member of a sorority/fraternity, attend religious services, live on campus, relationship status, current use of tobacco, alcohol, and lifetime use of other illicit drugs	Crude: 1.03 (1.01-1.05)

Association between Depression and Tobacco use						
Cross-Sectional Studies						
Lee Ridner, 2005, U.S. (39)	895	College students aged 18-24	Current/ non-users	CES-D, cut-off point of 16	-	Crude: 1.49 (1.18-1.90)
Susan Roberts, 2009, U.S. (31)	418	College students, aged 18-21	Current/ non-users	BDI-II, cut-off point of 20	-	Crude: 2.08 (1.29-3.36)
Elisabeth Simantov, 2000, U.S. (47)	5513	Grade 7-12 students	Regular/ non-users	Modified version of CDI, cut-off point of 9	-	Crude: 2.47 (2.06-2.97)
Sung Chung, 2014, U.S. (24)	11848	Grade 9-11 students	Current/ non-users	1 item question	-	Crude: 1.33 (1.16-1.53)
Shahm Martini, 2002, U.S. (45)	11201	Adolescents aged 12-17	Current/ non-users	YSR, cut-off point of 3	Age, ethnicity, school attendance, site, substance use behaviors	Crude: 1.83 (1.67-2.01)
Carla Berg, 2008, U.S. (46)	299	Adolescents aged 10-19	Current/ non-users	A 5-item question, cut-off point of 21	Age, sex, ethnicity, church attendance, perceived parental attitude	Crude: 3.83 (1.65-8.88)
Martha Kubik, 2005, U.S. (32)	3466	Grade 7 students	Current/ non-users	CES-D, cut-off point of 16	Age, ethnicity, SES, all other substance use behaviors	Adjusted: 1.56 (1.14-2.14)
Gilat Grunau, 2009, Canada (27)	6943	Students aged 13-18	Current/ non-users	Prescribed depression medications	Age, sex, ethnicity, parent(s), sibling(s), peer(s) smokes, anxiety	Adjusted: 2.59 (1.79-3.73)
Amanda Richardson, 2012, U.S. (48)	1884	Adolescents aged 12-15	Ever/ never users	NIMH-DISC-IV	Age, ethnicity, attending school, poverty index ratio, live with smokers, anxiety disorders	Adjusted: 2.80 (1.13-6.91)

Eleanor Hanna, 2001, U.S. (30)	719	Adolescents aged 12-16	Current/ non-users	Diagnostic interview schedule, DSM-III	Age, sex, ethnicity, family poverty status, school problem, drinking status	Adjusted: 0.98 (0.33-2.90)
Longitudinal studies: Tobacco use (exposure) → Depression (outcome)						
Brian Duncan, 2005, U.S. (40)	13068	Students grade 7-12, 1-year follow-up	Current/ non-users	CES-D, cut-off point of 22 (M) and 24 (F)	Disability, age, ethnicity, household, parental education, county-level variables	Crude: 2.37 (2.02-2.77)
Elizabeth Goodman, 2000, U.S. (41)	8704	Adolescents aged 11-22, 1-year follow-up	Current/ non-users	CES-D, cut-off point of 22 (M) and 24 (F)	Age, sex, ethnicity, parental education	Crude: 2.31 (1.83-2.92)
Katholiki Georgiades, 2007, Canada (49)	1282	Adolescents aged 12-16, 14-year follow-up	Daily/ non-users	CIDI-SF	Physical health, life satisfaction, personal income, years of education	Adjusted: 1.93 (1.01-3.70)
David Brook, 2002, U.S. (51)	736	Adolescents aged 14, A 13-year follow-up	Ever/ never users	Modified version of CIDI	Age, sex, parental educational level, family income, prior psychiatric disorders	Adjusted: 1.18 (1.01-1.39)
Longitudinal studies: Depression (exposure) → Tobacco use (outcome)						
Elizabeth Goodman, 2000, U.S. (41)	6947	Adolescents aged 11-22, 1-year follow-up	Current/ non-users	CES-D, cut-off point of 22 (M) and 24 (F)	Age, sex, ethnicity, education	Crude: 2.81 (1.67-4.74)
Kiyuri Naicker, 2012, Canada (50)	681	Adolescents aged 16-17, 10-year follow-up	Daily/ non-users	CIDI-SF, cut-off point of 5	Sex and SES	Adjusted: 2.89 (1.53-5.45)
Jie Wu Weiss, 2004, U.S. (36)	1699	Grade 6 students,	Ever/ never users	CES-D, cut-off point of 16	change in depression and hostility, sex, ethnicity, SES	Adjusted: 1.76 (1.30-2.38)

		A 1-year follow-up				
Jennifer Mendel, 2012, U.S. (37)	1205	Grade 10-11 students, A 5-year follow-up	Ever/ never users	CES-D, cut-off point of 16	Sex, parental marital status, family income, education level, marital status, children, GPA, delinquency, stressful life events, family support, quality of friendship, parental smoking, adolescent alcohol, cannabis use, extent of alcohol problems, peers who drink or use drugs, change in CESD and alcohol use	Adjusted: 0.97 (0.92-1.03)
Jennifer O'Loughlin, 2016, Canada (53)	690	Grade 5 students, 7-year follow-up	Ever/ never users	6-item question	Age, sex, mother's education	Adjusted: 1.34 (1.16-1.56)
Marcus Munafo, 2007, U.S. (38)	12149	Grade 7-12 students, 1-year follow-up	Ever/ never users	CES-D, cut-off point of 22 (M) and 24 (F)	Age, sex, ethnicity, depressed mood, parental/peer tobacco, alcohol use, delinquency score	Adjusted: 1.13 (1.03-1.25)
William Lechner, 2016, U.S. (42)	2460	Grade 9 students, A 1-year follow-up	Ever/ never users	CES-D, cut-off point of 22 (M) and 24 (F)	Age, sex, ethnicity, school, living situation, parental education, use of alcohol and other tobacco products	Adjusted: 1.02 (1.01-1.04)

Association between Anxiety and Alcohol use						
Cross-Sectional Studies						
Margo Villarosa, 2014, U.S. (28)	532	College students aged 18-22	Daily use, AUDIT	SIAS	-	Crude: 1.61 (1.29-2.00)
Meade Eggleston, 2003, U.S. (56)	284	College students aged 17-23	Binge/ non-drinkers	SIAS	-	Crude: 1.55 (1.15-2.10)
Esther Strahan, 2010, U.S. (57)	697	College students aged 17-27	AUDIT	SIAS	-	Crude: 1.04 (1.01-1.08)
Ping Wu, 2009, U.S. (58)	781	Adolescents aged 13-17	Frequent, heavy/non-drinkers	DISC	Age, ethnicity, public assistance, not living with parents, parental drug/alcohol problems, site	Adjusted: 1.74 (1.07-2.81)
Linda Richter, 2015, U.S. (25)	24445	Adolescents aged 12-20	Binge/ non-drinkers	Diagnosed anxiety (self-reported)	Age, sex, ethnicity	Adjusted: 1.54 (1.12-2.12)
Robert Roberts, 2007, U.S. (34)	4175	Adolescents aged 11-17	AUD	DISC-IV	Mood, conduct oppositional, and ADHD disorders.	Crude: 1.57 (0.72-3.40)
Nancy Low, 2008, U.S. (35)	632	Adolescents aged 13-19	AUD	PRIME-MD	Age, sex, ethnicity, sample site, mood disorders	Adjusted: 3.80 (1.21-11.91)
Longitudinal study: Anxiety (exposure) → Alcohol use (outcome)						
Julia Buckner, 2008, U.S. (59)	816	Students aged 15-17, 14-year follow-up	AUD	K-SADS	Sex, conduct, mood, CUDs, T1 AUD excluded	Adjusted: 2.16 (0.82-5.69)

Association between Anxiety and Cannabis use						
Cross-Sectional Studies						
Julia Buckner, 2008, U.S. (29)		College students aged 18-26	Frequent/ non-users	SIAS	-	Crude: 1.23 (0.88-1.73)
Robert Roberts, 2007, U.S. (34)	4175	Adolescents aged 11-17	CUD	DISC-IV	Mood, conduct oppositional, and ADHD disorders	Crude: 1.38 (0.70-2.75)
Nancy Low, 2008, U.S. (35)	632	Adolescents aged 13-19	CUD	PRIME-MD	Age, sex, ethnicity, sample site, mood disorders	Crude: 1.40 (0.40-4.70)
Longitudinal study: Anxiety (exposure) → Cannabis use (outcome)						
Julia Buckner, 2008, U.S. (59)	816	Students aged 15-17, 14-year follow-up	CUD	K-SADS	Sex, conduct, mood, AUDs, T1 CUD excluded	Adjusted: 3.28 (1.14-9.40)

Association between Anxiety and Cannabis use						
Cross-Sectional Studies						
Gilat Grunau, 2009, Canada (27)	6943	Students aged 13-18	Current/ non-users	Prescribed anxiety medications	Sex, ethnicity, age, parent(s), sibling(s), peer(s) smokes, depression	Adjusted: 1.83 (1.05-3.22)
Ping Wu, 2009, U.S. (58)	781	Adolescents aged 13-17	Daily/ non-users	DISC	Age, ethnicity, public assistance, not living with parents, parental drug/alcohol problems, site.	Adjusted: 3.14 (1.69-5.81)
Amanda Richardson, 2012, U.S. (48)	1884	Adolescents aged 12-15	Ever/ never users	NIMH-DISC-IV	Age, ethnicity, attending school, poverty index ratio, live with smokers, depressive disorder	Adjusted: 4.70 (1.61-13.75)
Longitudinal study: Tobacco use (exposure) → Anxiety (outcome)						
Renee Goodwin, 2005, U.S. (33)	940	Students aged 14-18, anxiety: young adults mean age 24.2	Ever, daily/ non-users	K-SADS	-	Crude: 1.88 (1.47-2.41)
Longitudinal study: Anxiety (exposure) → Tobacco use (outcome)						
Renee Goodwin, 2005, U.S. (33)	940	Students aged 14-18, tobacco use: young adults mean age 24.2	Ever, daily/ non-users	K-SADS	-	Crude: 1.38 (0.83-2.29)

Table 2.3: Pooled estimate (overall and by study design)

	Study Designs	N	OR (95% CI)	I^2% and p-value
Depression and Alcohol use	Overall	9	1.50 (1.24-1.83)	90.54, <0.001
	Cross-Sectional	6	1.57 (1.09-2.26)	92.89, <0.001
	Longitudinal: Alcohol use at baseline	2	1.39 (0.95- 2.03)	89.24, <0.001
	Longitudinal: Depression at baseline	1	1.78 (1.10-2.88)	n/a
Depression and Cannabis use	Overall	9	1.29 (1.10-1.51)	74.79, <0.01
	Cross-Sectional	3	1.34 (0.97-1.84)	53.26, 0.12
	Longitudinal: Cannabis use at baseline	5	1.33 (1.19-1.49)	0.00, 0.53
	Longitudinal: Depression at baseline	1	1.03 (1.01-1.05)	n/a
Depression and Tobacco use	Overall	20	1.65 (1.43-1.92)	96.23, <0.01
	Cross-Sectional	10	1.87 (1.55-2.25)	78.60, <0.01
	Longitudinal: Tobacco use at baseline	4	1.87 (1.23-2.85)	92.95, <0.01
	Longitudinal: Depression at baseline	7	1.22 (1.09-1.37)	89.56, <0.001
Anxiety and Alcohol use	Overall	8	1.54 (1.19-2.00)	81.52, <0.001
	Cross-Sectional	7	1.51 (1.16-1.97)	83.28, <0.001
	Longitudinal: Alcohol use at baseline	-	-	-
	Longitudinal: Anxiety at baseline	1	2.16 (0.82-5.69)	n/a
Anxiety and Cannabis use	Overall	4	1.36 (1.02-1.81)	0.39, 0.39
	Cross-Sectional	3	1.27 (0.94-1.70)	0.00, 0.94
	Longitudinal: Cannabis use at baseline	-	-	-
	Longitudinal: Anxiety at baseline	1	3.28 (1.14-9.40)	n/a
Anxiety and Tobacco use	Overall	4	2.21 (1.54-3.17)	46.17, 0.13
	Cross-Sectional	3	2.67 (1.62-4.37)	33.12, 0.22
	Longitudinal: Tobacco use at baseline	1	1.88 (1.47-2.41)	n/a
	Longitudinal: Anxiety at baseline	1	1.38 (0.83-2.29)	n/a

Table 2.4: Subgroup Analysis

Subgroup Analysis			N	OR (95% CI)	I^2% and p-value	p-value
Depression and Alcohol use	Point Estimate	Crude	3	1.37 (0.87-2.18)	96.08, <0.001	0.56
		Adjusted	6	1.62 (1.19-2.19)	84.60, <0.001	
	Target Population	Adolescents	7	1.69 (1.28-2.25)	90.63, <0.001	0.28
		Young adults	3	1.28 (0.83-1.97)	82.52, <0.001	
	Severity of MHDs[1]	Symptoms	5	1.37 (1.08-1.75)	94.04, <0.001	0.21
		Disorders	4	1.67 (1.38-2.02)	14.68, 0.32	
	Intensity of substance use	Not binge drinkers	6	1.61 (1.29-2.01)	79.79, <0.001	0.06
		Binge drinkers	6	1.21 (0.99-1.47)	87.67, <0.001	
Depression and Cannabis use	Point Estimate	Crude	3	1.27 (0.95-1.69)	80.29, <0.001	0.85
		Adjusted	6	1.31 (1.17-1.46)	0.00, 0.48	
	Target Population	Adolescents	6	1.34 (1.17-1.54)	9.96, 0.35	0.46
		Young adults	4	1.22 (0.99-1.51)	72,62, 0.01	
	Severity of MHDs	Symptoms	5	1.20 (1.01-1.42)	73.16, <0.001	0.16
		Disorders	4	1.41 (1.21-1.65)	0.00, 0.60	
	Intensity of substance use	Cannabis use	7	1.25 (1.06-1.47)	77.10, <0.001	0.23
		CUD[2]	2	1.63 (1.09-2.44)	0.00, 0.42	
Depression and Tobacco use	Point Estimate	Crude	8	1.99 (1.65-2.40)	86.62, <0.001	<0.001
		Adjusted	12	1.30 (1.16-1.45)	87.12, <0.001	
	Target Population	Adolescents	18	1.67 (1.43-1.96)	96.56, <0.001	0.40
		Young adults	3	1.37 (0.89-2.12)	84.18, <0.001	
	Severity of MHDs	Symptoms	14	1.61 (1.36-1.89)	97.18, <0.001	0.48
		Disorders	6	1.91 (1.22-2.97)	78.86, <0.001	
	Intensity of substance use	Ever smokers	7	1.14 (1.04-1.25)	84.89, <0.001	<0.001
		Current smokers	14	1.90 (1.62-2.23)	82.65, <0.001	
Anxiety and Alcohol use	Point Estimate	Crude	4	1.37 (1.00-1.88)	86.27, <0.001	0.3
		Adjusted	4	1.70 (1.32-2.18)	0.00, 0.47	
	Target Population	Adolescents	5	1.69 (1.33-2.14)	0.00, 0.64	0.29
		Young adults	3	1.35 (0.96-1.90)	90.40, <0.001	
	Severity of MHDs	Symptoms	3	1.35 (0.96-1.90)	90.40, <0.001	0.29
		Disorders	5	1.69 (1.33-2.14)	0.00, 0.64	
	Intensity of substance use	Alcohol use	6	1.49 (1.26-1.76)	0.00, 0.88	0.59
		AUD[3]	5	1.71 (1.05-2.79)	83.88, <0.001	
Anxiety and Cannabis use	Point Estimate	Crude	2	1.26 (0.93-1.71)	0.00, 0.76	0.19
		Adjusted	2	2.28 (1.00-5.20)	5.37, 0.30	
	Target Population	Adolescents	3	1.71 (1.02-2.89)	0.00, 0.38	0.29
		Young adults	1	1.23 (0.88-1.73)	n/a	
	Severity of MHDs	n/a				

	Intensity of substance use	Cannabis use	1	1.23 (0.88-1.73)	n/a	0.29
		CUD	3	1.71 (1.02-2.89)	0.00, 0.38	
Anxiety and Tobacco use	Point Estimate	Crude	1	1.78 (1.42-2.22)	n/a	0.14
		Adjusted	3	2.67 (1.62-4.37)	33.125, 0.22	
	Target Population	n/a				
	Severity of MHDs	n/a				
	Intensity of substance use	Ever	3	1.62 (0.67-3.92)	69.87, 0.04	0.58
		Current	4	2.10 (1.69-2.62)	0.00, 0.52	
[1] Mental Health Disorders, [2] Cannabis Use Disorder, [3] Alcohol Use Disorder						

Figure 2.1: PRISMA Diagram

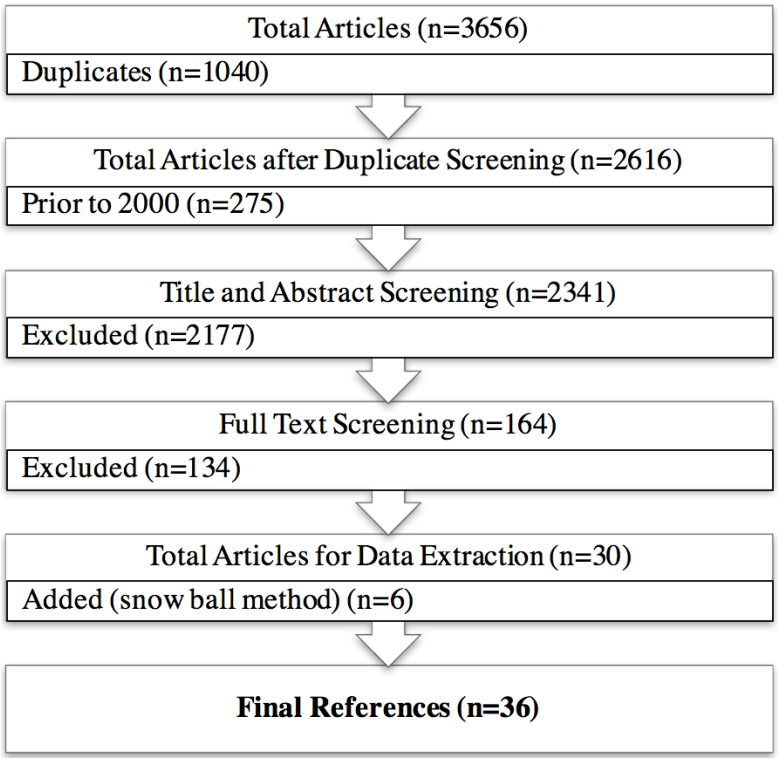
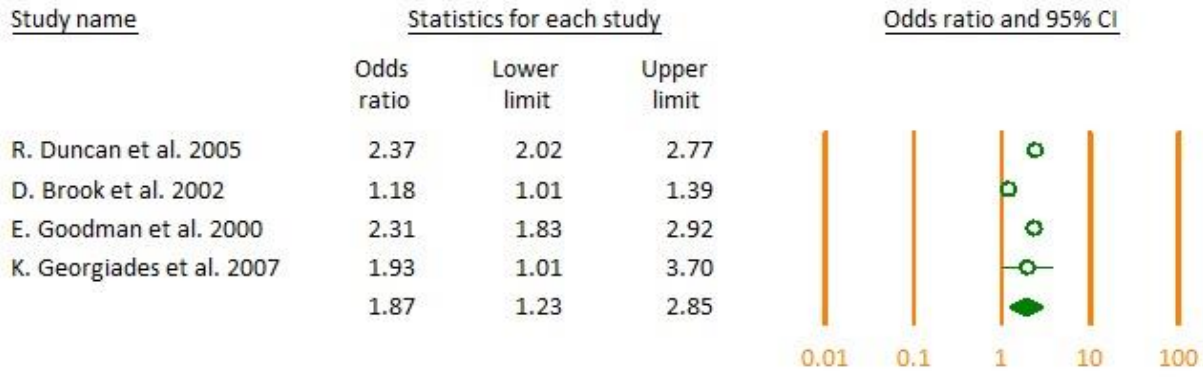


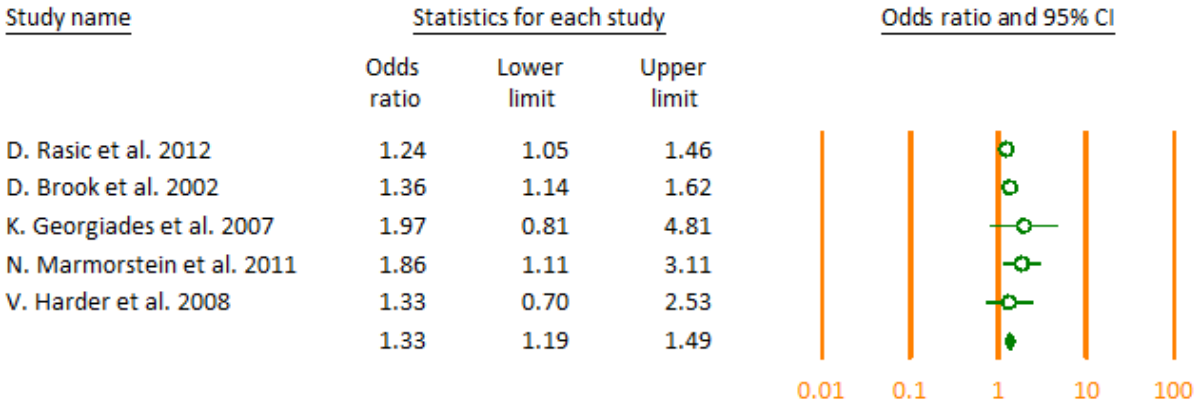
Figure 2.2: Examining the directionality in longitudinal studies (Forest plots)

The association between tobacco use at baseline and depression at follow-up



The association between depression at baseline and tobacco use at follow up

The association between cannabis use at baseline and depression at follow up



Chapter 3: Examining the association between mental health disorders and substance use among Canadian post-secondary students

3.1 Abstract

Background: Mental health disorders and substance use are reported to be common among post-secondary students. Co-occurrence of mental health disorders and substance use may be due to a number of inter-complex but closely inter-linked factors. In Canada, the independent association between mental health disorders and substance use is not clearly established. Therefore, the purpose of this study was to examine the association between mental health disorders and substance use among Canadian post-secondary students.

Methods: This study was conducted using the spring 2016, ACHA-NCHA II survey. It includes 43,780 college students from 41 Canadian post-secondary institutions. The exposure variables of interest were alcohol, cannabis, and tobacco use and the outcome variables of interest were diagnosis or treatment for depression and/or anxiety. Descriptive statistics, univariate and multivariate logistic regression models were used to analyze our data.

Results: Our study found that 14.7% of post-secondary students were diagnosed or treated for depression and 18.4% for anxiety within the past 12-months. Among current (past 30-days) substance use, it was reported that alcohol (69.3%), cannabis (17.9%), and tobacco (11%) were the most common. There was a significant association between depression and current tobacco use (OR=1.36, 95% CI: 1.22-1.52, $p<0.001$) and current cannabis use (OR=1.17, 95% CI: 1.05-1.31, $p<0.001$). There was also a gender-specific association between anxiety and female alcohol users (OR=1.41, 95% CI: 1.24-1.62, $p<0.001$).

Conclusion: The results of this study showed significant associations between depression, tobacco use and cannabis use, and anxiety and alcohol use in females. These conditions should be screened concurrently for improved outcomes. Results of this study may help inform student health services, university administrators, and healthcare professionals in their efforts to design and implement comprehensive educational initiatives, appropriate policies, and effective health promotion strategies.

Keywords: Depression, anxiety, alcohol, cannabis, tobacco, post-secondary students

3.2 Introduction

For many, young adulthood is a critically important time in their lives as they transition from high school to post-secondary studies to pursue greater educational opportunities, develop personal relationships, and achieve their career goals. Post-secondary education provides students with many opportunities and challenges for their personal development and growth. Among the challenges faced are increased independence and responsibility that may at times, lead to highly stressful situations. The competitive nature and pressurized academic environment of post-secondary education makes some students vulnerable to develop mental health disorders and/or substance use problems either independently or concurrently (1). These conditions may affect their academic progress, personal development, and professional life.

The prevalence of mental health disorders among post-secondary students is estimated to be approximately 20%, worldwide (2). Anxiety (11.7%) and depressive disorders (4.5%) were the two most common mental health disorders found in this population (2). Despite the high proportion of students affected by mental health disorders, a considerable number are undiagnosed and/or do not receive adequate treatment (2). Students with mental health disorders (such as anxiety or depressive disorders) encounter difficulties on a personal (academic performance and coping abilities), interpersonal (ability to handle work/life responsibilities and engagement in social activities), and institutional (time to graduation and graduation rate) level, which negatively impacts their health and well-being (3, 4).

Another serious problem facing post-secondary students is substance use. Alcohol, cannabis, and tobacco are the three most common substances used among post-secondary students (5). In Canada, the prevalence of current alcohol (83%), cannabis (30%), and tobacco (18%) use is highest among individuals aged 20-24 years old, a large proportion of whom are post-secondary students (6). College students may use substances as a way to escape from school/work/financial stresses, social pressures, and as a means to compensate for feelings of shyness, inadequacy or low self-esteem. However, substance use is reported to lead to several adverse outcomes including poor academic performance (7), unintentional injuries (8), and increased engagement in other risky behaviors (9, 10).

Mental health disorders and substance use are closely linked and pose a growing public health concern for many university campuses across Canada. It is reported that individuals with concurrent disorders experience more serious medical, social, and emotional problems (11). Affected individuals are also more often refractory to treatments and require more extensive healthcare support (12). Mental health disorders and substance use can co-occur due to a variety of reasons including 1) common risk factors (such as biological factors or traumatic events); 2) self-medication hypothesis (individuals already suffering from mental health disorders may exhibit a maladaptive response and self-medicate by using substances to forget bad feelings, problems, and to relieve symptoms of their mental health disease); 3) substance use-induced mental health problems (individuals may develop a mental health problem as a direct [i.e., pharmacogenic] consequence of their substance use); and 4) substance use-related mental health problems (individuals may develop a mental health problem as an indirect [i.e., socio-economic stressors, unemployment, dysfunctional relationships] consequence of their substance use) (11). However, due to the multifactorial nature of this problem, it is not yet clear whether an independent association exists between mental health disorders and substance use as the literature reports inconsistent findings (13-16).

There has been considerable attention given to mental health disorders and substance use among high school students; however, less is known about post-secondary students. Moreover, much of the published research examining the association between mental health disorders and substance use has been conducted in countries other than Canada. Therefore, the purpose of this study was

to examine the association between mental health disorders and substance use among Canadian post-secondary students.

3.3 Methods

This study used data from the American College Health Association - National College Health Assessment II (ACHA-NCHA II) - Canadian Reference Group survey, spring 2016. The population of interest in this national survey was post-secondary students. The 2016, ACHA-NCHA II survey consists of data from 43,780 students representing 41 Canadian post-secondary institutions. These institutions either surveyed all their students or used a representative random sampling method. The overall participation rate was 19.2% (5).

3.3.1 Outcome variables

The outcome variables of interest in this study were: 1) history of depression (yes/no), and 2) history of anxiety (yes/no). Respondents were specifically asked to indicate whether they had: 1) been diagnosed or treated by a medical professional for depression within the past 12-months, and/or 2) been diagnosed or treated by a medical professional for anxiety within the past 12-months.

3.3.2 Explanatory variables

Substance use was the primary exposure of interest. The three variables analysed were: 1) alcohol use (never/former/current user), 2) cannabis use (never/former/current user), and 3) tobacco use (never/former/current user). Responses were re-categorised to 1) never users (never used the substance), 2) former users (used the substance but not within the past 30-days), and 3) current users (used the substance within the past 30-days).

3.3.3 Demographics and Other Factors

Sociodemographic variables and other factors were reported in this study. The gender variable had three levels: male, female, and non-binary (those who cannot describe themselves as solely

male or female). Age groups were re-categorised as follows: 1) 18 to 20 years old, 2) 21 to 23 years old, and 3) 24 years old or older. Ethnicity was self-reported from the following question: Do you usually describe yourself as White, Black, Hispanic/Latino, Asian/Pacific Islander, American Indian/Alaskan Native/Native Hawaiian, Biracial/Multiracial, or Other? Participants were also asked about their marital status (single, married, separated/divorced, or other). Additionally, there were questions that described the following: international student (yes/no), housing (live with their parents/on-campus/off-campus), enrollment status (full-time/part-time/other), study status (undergraduate/graduate/other), and Grade Point Average (GPA) (A/B/C/D or F/not applicable).

Questions pertaining to other substance use (never/former/current user) included: cocaine, methamphetamine, sedatives, hallucinogens, opiates, inhalants, MDMA, and other club and illegal drugs. Participants were then re-categorized into three groups: 1) never users (never used any of the other substances), 2) former users (used but not within the past 30-days), and 3) current users (used within the past 30-days). Questions pertaining to other mental health disorders (yes/no) were re-categorised based on participant's response to the following questions: Have you been diagnosed or treated by a medical professional for any of the following mental health disorders: anorexia, attention-deficit hyperactivity disorder (ADHD), bipolar disorder, bulimia, insomnia, and schizophrenia within the past 12-months. If yes, the participant was coded as yes for the other mental health disorders variable.

3.3.4 Data analysis

All statistical analyses were computed using SAS version 9.4. Descriptive statistics for the exposure and outcome variables of interest and other co-variates were examined (Table 3.1). Univariate analysis was conducted to assess the crude association of one explanatory variable at a time with the outcome variable of interest (depression or anxiety) (Table 3.2). During univariate analysis, variables with a significance level of less than 0.15 were screened and were included in the multivariate analysis.

Two separate multivariable logistic regression (MLR) models were built using depression and anxiety as the outcomes of interest. Both models used substance use behavior (alcohol, cannabis, and tobacco use) as the main exposures while controlling for demographic characteristics and other factors as presented in Table 3.3. Multicollinearity among independent variables was assessed using the Variance Inflation Factor (VIF<2.5 indicated no multicollinearity). Backward selection strategy was used to build the final models. The confounding effect of statistically insignificant variables was assessed before they were removed from the models. A change of 10% or more in the regression coefficient of the primary predictor suggested that the variable is a confounder. All potential two-way interactions were assessed using a level of significance of 0.05 (α=0.05). A diagnostic test (AIC value) was used to check goodness of fit comparing the full model with and without the interaction terms. ROC curves were graphed to check the ability of the two logistic regression models to predict the probability of depression and anxiety.

3.4 Results

3.4.1 Descriptive statistics

Of the 43,780 post-secondary students, 14.7% were diagnosed or treated by a medical professional for depression and 18.4% for anxiety within the past 12-months. Among substance use, alcohol (69.3%), cannabis (17.9%), and tobacco use (11%) were most common in the past 30-days. The majority of participants were female (67.9%), white (70.7%), ages 18-20 years old (40.3%), single (83%), undergraduate students (83.2%), domestic (90.6%), living off-campus (53.3%), studying full-time (93.3%), and with a GPA of B (45.1%). Table 3.1 provides detailed descriptive statistics of the study population.

3.4.2 Univariate analysis

Participants reporting current (past 30-day) alcohol use were 1.74 (95% CI: 1.60-1.90) times more likely than those who never used alcohol to report depression. Participants reporting current cannabis use were 2.23 (95% CI: 2.08-2.38) times more likely than those who never used cannabis to report depression. Individuals reporting current tobacco use were 2.49 (95% CI: 2.31-2.68) times more likely than those who never used tobacco to report depression. Table 3.2

presents the univariate analysis examining depression and substance use variables, and other risk factors.

When examining the unconditional association between substance use and anxiety, participants who were current alcohol users were 1.92 (95% CI: 1.77-2.08) times more likely to report anxiety compared to those who never used alcohol. Participants who were current cannabis users were 2.00 (95% CI: 1.88-2.13) times more likely to report anxiety compared to those who never used cannabis. Finally, participants who were current tobacco users were 2.04 (95% CI: 1.90-2.19) times more likely than those who never used tobacco to report anxiety. Table 3.3 summarizes the univariate analysis examining anxiety and substance use variables, and other risk factors.

3.4.3 Multivariate analysis

Two multivariate logistic regression models were built for the two outcomes of interest (depression and anxiety).

Model 1: depression and substance use

Findings of our model for depression showed that the odds of having depression were greater for current tobacco users (OR=1.36, 95% CI: 1.22-1.52) and to a lesser extent former tobacco users (OR=1.20, 95% CI: 1.09-1.33) compared to never tobacco users. An interaction effect was observed between cannabis use and other mental health disorders. Current cannabis users with (OR=1.17, 95% CI: 1.05-1.31) or without (OR=1.29, 95% CI: 1.05-1.57) other mental health disorders were more likely to have depression compared to never cannabis users. Former cannabis users without other mental health disorders were more likely to have depression (OR=1.38, 95% CI: 1.16-1.65) compared to never cannabis users.

The odds of having depression were increased for current users of other substances (OR=1.37, 95% CI: 1.21-1.55) and former users of other substances (OR=1.23, 95% CI: 1.10-1.36) compared to never users of other substances; females (OR=1.39, 95% CI: 1.28-1.51) and non-

binary (OR=2.10, 95% CI: 1.75-2.52) gendered individuals compared to males; participants ages 24 years old and older compared to those ages 18-20 years old (OR=1.21, 95% CI:1.09-1.34); divorced students compared to single students (OR=1.58, 95% CI: 1.22-2.04); part-time compared to full-time students (OR=1.34, 95% CI: 1.17-1.54); undergraduate compared to graduate students (OR=1.19, 95% CI: 1.06-1.35); and individuals reporting a GPA of D or F compared to those with a GPA of A (OR=1.79, 95% CI: 1.39-2.31). The following variables were excluded from the final model: alcohol use, ethnicity, housing, and being an international student (Table 3.4).

Model 2: anxiety and substance

There was an interaction in the final model between alcohol use and gender. The odds of having anxiety were 41% greater for female current alcohol users (OR=1.41, 95% CI: 1.24-1.62) and 43% for female former alcohol users (OR=1.43, 95% CI: 1.22-1.68) compared to female non-alcohol users. The odds of having been diagnosed with anxiety was increased for current users of other substances (OR=1.28, 95% CI: 1.14-1.45) compared to never users of other substances; students ages 21-23 years old compared to those ages 18-20 years old (OR=1.18, 95% CI: 1.08-1.28); and for those with other mental health disorders (OR=50.77, 95% CI: 47.10-54.72) compared to those without other mental health disorders.

The odds of having been diagnosed with anxiety were decreased among Black (OR=0.59, 95% CI: 0.46-0.75) and Asian or Pacific Islander (OR=0.59, 95% CI: 0.52-0.67) students compared to White students. Married students were 14% less likely (OR=0.86, 95% CI: 0.77-0.96) to have an anxiety disorder compared to single students. The following variables were excluded from the final model: tobacco use, cannabis use, housing status, and study status (Table 3.5).

3.5 Discussion

Our study is among the first to examine the association between mental health disorders and substance use among post-secondary students in Canada. Specifically, we found a higher rate of depression and anxiety (14.7% and 18.4%) in 2016 compared to data from 2013 (10.0 and12.3%) among post-secondary students) (17). Similarly, increasing trends were observed with alcohol (83.6% in 2013 to 84.4% in 2016) and cannabis use (39.9% in 2013 to 41.6% in 2016) (17). Encouragingly, there was a decrease in tobacco use (29.2% in 2013 to 26.9% in 2016) (17). Overall, substance use remains a serious public health concern and is highly prevalent among Canadian post-secondary students.

There was an initial statistically significant association between depression and alcohol use in our univariate analysis. However, in our final model, depression was not significantly associated with alcohol use. This provides evidence in support of previous studies, which did not find an association between depression and alcohol use among post-secondary students (16, 18). However, other studies contradict our finding but were mainly focused in scope to the adolescent student population (19, 20). Age may play a critical role in this association as the harmful effects of alcohol use and/or depression may differentially impact adolescents (i.e., high school students) compared to young adults (post-secondary students) (21, 22). Evidence suggests that underage alcohol use is associated with neurodegeneration, changes in functional brain activity, and neurocognitive impairments leading to the development of mental health disorders such as depression (21). There is also a social context to the patterns of alcohol use. Among young adults, alcohol is oftentimes a social behavior, whereas, for adolescents, it may be used as a means of coping with underlying problems such as depression or anxiety (22).

Depression was associated with an interaction between cannabis use and other mental health disorders. Previous studies found a significant association between depression and cannabis use but without an interaction (18, 23). This could be due to a variety of reasons including the composition of the study population, cultural and geographical disparities, and differences in key characteristics among the various studies. The association between depression and cannabis use could be attributed to either direct and/or indirect factors. Direct factors linking depression and cannabis use include having a genetic predisposition to both conditions and biological

mechanisms altering neurochemical activities in the brain (24). However, another explanation is that an individual's maladaptive cognitive and coping styles (such as own-perception, social relationships, and coping with undesirable life events) may lead to occurrence of both depression and cannabis use (25).

Our results revealed a significant association between depression and tobacco use. This finding is consistent with previous studies that suggest an association exists between depression and current smoking among post-secondary students (18, 23). In our study, both current and former smokers were more likely to be diagnosed with depression compared to never smokers. However, there was no statistically significant difference between current and former smokers. This is an important finding as it suggests that former smokers are at similar risk of depression as current smokers. There may be a biological explanation for this finding. Smoking initially increases the release of dopamine neurotransmitters, which eventually may cause the receptors to become insensitive and therefore, over time may require an increased stimulation to have the same effect (26). Upon smoking cessation, due to the deprivation of dopamine and the occurrence of withdrawal symptoms, the depressive symptoms may develop (26). Thus, healthcare providers at post-secondary institutions should be made aware of the risk of depression not only among current but also former smokers.

Anxiety was associated with an interaction between alcohol use and gender. Females who used alcohol (current and former users) were at an increased risk of self-reported anxiety compared to never users. This is in accordance with a previous study found a stronger association between anxiety and alcohol use among females (27). Anxiety among male and non-binary participants was not associated with alcohol use. These findings highlight the notion that to improve mental health disorders and substance use outcomes, interventions should be gender-specific, relatable, and account for the different risk profiles among the genders.

3.6 Strengths and limitations

This study has several strengths. Our dataset was recent and had a large, national sample size. It investigated the characteristics and risk factors of two of the most common mental health disorders (depression and anxiety). Our population of interest was uniquely focused on post-

secondary students. Finally, this is one of the few studies examining the association between mental health disorders and substance use among post-secondary students in Canada.

The study also has a few limitations. The NCHA-ACHA II, spring 2016 survey is drawn from a convenience sample and results may not be entirely generalizable. The survey questions regarding mental health disorders and substance use were self-reported, and due to the private nature of the questions and possible associated social stigma, there may be some degree of underreporting by the participants. However, previous studies have shown that the use of self-reports for risky health behaviors are accurate and valid (28). Finally, this is a cross-sectional study, and we cannot infer causation because temporality is not known.

3.7 Conclusion

This study examined the association between mental health disorders and substance use among post-secondary students in Canada. A significant association was found between depression, tobacco use and cannabis use and a gender-specific association between anxiety and female alcohol users. Interventions that increase awareness and help fight the growing perception of substance use as a normalized and accepted behavior among post-secondary students may help to alleviate issues related to mental health disorders. Results of this study may help inform student health services, university administrators, and healthcare professionals in their efforts to design and implement comprehensive educational initiatives, appropriate policies, and effective health promotion strategies.

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Table 3.1: Descriptive statistics

Variables	Categories	Frequency	(%)
Depression (missing=539)	No	36896	85.33
	Yes	6345	14.67
Anxiety (missing=495)	No	35328	81.62
	Yes	7957	18.38
Other mental health disorders (missing=320)	No	32812	75.50
	Yes	10648	24.50
Alcohol use (missing=336)	Never[1]	6761	15.56
	Former[2]	6567	15.12
	Current[3]	30116	69.32
Cannabis use (missing =399)	Never	25350	58.44
	Former	10261	23.65
	Current	7770	17.91
Tobacco use (missing=306)	Never	31780	73.10
	Former	6913	15.90
	Current	4781	11.00
Other substances (missing=196)	Never	35534	81.53
	Former	5292	12.14
	Current	2758	6.33
Gender (missing=558)	Male	12615	29.19
	Female	29359	67.93
	Non-binary	1248	2.89
Ethnicity (missing=578)	White	30561	70.74
	Black	1402	3.25
	Hispanic/Latino	888	2.06
	Asian/Pacific Islander	5905	13.67
	Indian	1701	3.94
	Biracial/multiracial	1462	3.38
	Other	1283	2.97
Age (missing=536)	18-20	17419	40.28
	21-23	13955	32.27
	24 years and older	11870	27.45
Marital status (missing =442)	Single	35966	82.99
	Married	5498	12.69
	Separated/Divorced	547	1.26
	Others	1327	3.06
Study status (missing=505)	Undergraduate	36021	83.24
	Graduate	6026	13.92
	Others	1228	2.84
International student (missing=402)	No	39284	90.56
	Yes	4094	9.44
Housing (missing=398)	Off-Campus	23141	53.34
	On-Campus	6106	14.07

	With Parents	14135	32.58
Enrollment (missing=320)	Full-time	40528	93.25
	Part-time	2454	5.65
	Others	478	1.10
GPA (missing=432)	A	15799	36.45
	B	19562	45.13
	C	6619	15.27
	D/F	626	1.44
	Not Applicable	742	1.71

[1]Never users: Never used the substance
[2]Former users: Used the substance but not within the past 30-days
[3]Current users: Used the substance within the past 30-days

Table 3.2: Univariate analysis: Substance use and depression

Variables	Categories	OR (95% CI)	P-value
Other mental health disorders (Ref=no)	Yes	45.52 (41.99-49.34)	<0.001
Alcohol use (Ref=never[1])	Former[2]	1.68 (1.51-1.87)	<0.001
	Current[3]	1.74 (1.60-1.90)	
Cannabis use (Ref=never)	Former	1.71 (1.60-1.82)	<0.001
	Current	2.23 (2.08-2.38)	
Tobacco use (Ref=never)	Former	1.86 (1.74-1.99)	<0.001
	Current	2.49 (2.31-2.68)	
Other substances (Ref=never)	Former	2.16 (2.01-2.32)	<0.001
	Current	3.63 (3.33-3.96)	
Gender (Ref=male)	Female	1.79 (1.68-1.92)	<0.001
	Non-binary	3.89 (3.40-4.46)	
Age categories (Ref=age 18-20)	21-23	1.10 (1.03-1.17)	<0.001
	24 years and older	1.34 (1.26-1.43)	
Ethnicity (Ref=white)	Black	0.58 (0.49-0.70)	<0.001
	Hispanic or Latino	0.89 (0.73-1.08)	
	Asian or Pacific Islander	0.53 (0.48-0.58)	
	Indian	1.56 (1.38-1.75)	
	Biracial or multiracial	1.27 (1.11-1.46)	
	Other	1.01 (0.86-1.18)	
Marital status (Ref=single)	Married	1.07 (0.99-1.16)	<0.001
	Separated/Divorced	2.98 (2.48-3.57)	
	others	1.43 (1.24-1.64)	
Housing (Ref=on-campus)	Off-Campus	1.19 (1.10-1.29)	<0.001
	With Parents	0.95 (0.87-1.04)	
Enrollment status (Ref=full-time)	Part-time	1.58 (1.43-1.75)	<0.001
	Others	1.66 (1.33-2.07)	
Study status (Ref=graduate students)	Undergraduate students	1.29 (1.18-1.40)	<0.001
	Others	1.72 (1.47-2.03)	
GPA (Ref=A)	B	1.21 (1.14-1.29)	<0.001
	C	1.74 (1.61-1.88)	
	D/F	2.48 (2.06-2.98)	
	Not Applicable	1.27 (1.03-1.56)	
International student (Ref=no)	Yes	0.65 (0.59-0.72)	<0.001

[1]Never users: Never used the substance
[2]Former users: Used the substance but not within the past 30-days
[3]Current users: Used the substance within the past 30-days

Table 3.3: Univariate analysis: Substance use and anxiety

Variables	Categories	OR (95% CI)	P-value
Other mental health disorders (Ref=no)	Yes	54.21 (50.47-58.22)	<0.001
Alcohol use (Ref=never[1])	Former[2]	1.80 (1.63-1.98)	<0.001
	Current[3]	1.92 (1.77-2.08)	
Cannabis use (Ref=never)	Former	1.62 (1.53-1.72)	<0.001
	Current	2.00 (1.88-2.13)	
Tobacco use (Ref=never)	Former	1.64 (1.54-1.74)	<0.001
	Current	2.04 (1.90-2.19)	
Other substances (Ref=never)	Former	1.90 (1.78-2.03)	<0.001
	Current	3.18 (2.93-3.46)	
Gender (Ref=male)	Female	2.29 (2.15-2.44)	<0.001
	Non-binary	4.07 (3.57-4.64)	
Age categories (Ref=age 18-20)	21-23	1.16 (1.09-1.22)	<0.001
	24 years and older	1.20 (1.13-1.27)	
Ethnicity (Ref=white)	Black	0.42 (0.35-0.51)	<0.001
	Hispanic or Latino	0.79(0.66-0.94)	
	Asian or Pacific Islander	0.41 (0.37-0.45)	
	Indian	1.32 (1.18-1.48)	
	Biracial or multiracial	1.23 (1.08-1.39)	
	Other	0.94 (0.81-1.08)	
Marital status (Ref=single)	Married	0.99 (0.92-1.07)	<0.001
	separated/Divorced	2.49 (2.09-2.98)	
	others	1.38 (1.21-1.57)	
Housing (Ref=on-campus)	Off-Campus	1.12 (1.04-1.21)	<0.001
	With Parents	0.96 (0.88-1.03)	
Enrollment status (Ref=full-time)	Part-time	1.43 (1.30-1.58)	<0.001
	Others	1.54 (1.25-1.90)	
Study status (Ref=graduate students)	Undergraduate students	1.24 (1.15-1.33)	<0.001
	Others	1.45 (1.24-1.69)	
GPA (Ref=A)	B	1.10 (1.04-1.16)	<0.001
	C	1.42 (1.32-1.52)	
	D/F	1.73 (1.44-2.08)	
	Not Applicable	1.07 (0.88-1.30)	
International student (Ref=no)	Yes	0.55 (0.50-0.61)	<0.001

[1]Never users: Never used the substance
[2]Former users: Used the substance but not within the past 30-days
[3]Current users: Used the substance within the past 30-days

Table 3.4: Multivariate analysis: Substance use and depression

Variables	Categories	OR (95% CI)	P-value
Tobacco use (Ref=never[1])	Former[2]	1.20 (1.09-1.33)	<0.001
	Current[3]	1.36 (1.22-1.52)	<0.001
Other substances use (Ref=never)	Former	1.23 (1.10-1.36)	<0.001
	Current	1.37 (1.21-1.55)	<0.001
Gender (Ref=male)	Female	1.39 (1.28-1.51)	<0.001
	Non-binary	2.10 (1.75-2.52)	<0.001
Age categories (Ref=age 18-20)	21-23	1.00 (0.92-1.09)	0.98
	24 years and older	1.21 (1.09-1.34)	0.003
Marital status (Ref=single)	Married	0.98 (0.87-1.10)	0.72
	Divorced	1.58 (1.22-2.04)	0.005
	others	1.07 (0.89-1.29)	0.49
Enrollment status (Ref=full-time)	Part-time	1.34 (1.17-1.54)	<0.001
	Others	1.26 (0.93-1.71)	0.13
Study status (Ref=graduate students)	Undergraduate students	1.19 (1.06-1.35)	0.005
	Others	1.46 (1.17-1.82)	<0.001
GPA (Ref=A)	B	1.13 (1.04-1.23)	0.003
	C	1.53 (1.37-1.70)	<0.001
	D/F	1.79 (1.39-2.31)	<0.001
	Not Applicable	1.19 (0.91-1.57)	0.21

Variables	Categories	OR (95% CI)
Other Mental Health Disorders=0		
Cannabis use (Ref=never)	Former	1.38 (1.16-1.65)
	Current	1.29 (1.05-1.57)
Other Mental Health Disorders=1		
Cannabis use (Ref=never)	Former	1.06 (0.95-1.17)
	Current	1.17 (1.05-1.31)

[1]Never users: Never used the substance
[2]Former users: Used the substance but not within the past 30-days
[3]Current users: Used the substance within the past 30-days

Table 3.5: Multivariate analysis: Substance use and anxiety

Variables	Categories	OR (95% CI)	P-value
Other substances use (Ref=never[1])	Former[2]	1.09 (0.98-1.20)	0.08
	Current[3]	1.28 (1.14-1.45)	0.002
Age categories (Ref=age 18-20)	21-23	1.18 (1.08-1.28)	<0.001
	24 years and older	1.01 (0.92-1.11)	0.66
Ethnicity (Ref=white)	Black	0.59 (0.46-0.75)	<0.001
	Hispanic or Latino	0.79 (0.62-1.01)	0.06
	Asian or Pacific Islander	0.59 (0.52-0.67)	<0.001
	Indian	0.89 (0.76-1.05)	0.13
	Biracial or multiracial	1.07 (0.90-1.28)	0.51
	Other	0.90 (0.74-1.10)	0.22
Marital Status (Ref=single)	Married	0.86 (0.77-0.96)	0.01
	Divorced	1.24 (0.95-1.62)	0.09
	others	1.02 (0.84-1.23)	0.82
Enrollment Status (Ref=full-time)	Part-time	1.23 (1.07-1.42)	0.00
	Others	1.33 (0.97-1.81)	0.07
GPA (Ref=A)	B	0.91 (0.84-0.99)	0.02
	C	1.06 (0.96-1.18)	0.32
	D/F	0.92 (0.71-1.20)	0.53
	Not Applicable	1.03 (0.78-1.36)	0.94
International Student (Ref=yes)	No	1.32 (1.15-1.53)	<0.001
Other Mental Health Disorders (Ref=no)	Yes	50.77 (47.10-54.72)	<0.001

Variables	Categories	OR (95% CI)
Female		
Alcohol use (Ref=never)	Former	1.43 (1.22-1.68)
	Current	1.41 (1.24-1.62)
Male		
Alcohol use (Ref=never)	Former	1.27 (0.97-1.68)
	Current	0.97 (0.78-1.20)
Non-binary		
Alcohol use (Ref=never)	Former	1.56 (0.84-2.89)
	Current	1.65 (0.98-2.76)

[1]Never users: Never used the substance
[2]Former users: Used the substance but not within the past 30-days
[3]Current users: Used the substance within the past 30-days

Chapter 4: Conclusion

4.1 Overview

Mental health disorders and substance use pose a major public health concern. These two conditions contribute a significant portion of world's disease burden measured by disability-adjusted life years (1). The majority of mental health disorders and substance use behaviors, often times, emerge during adolescence and young adulthood (2). Early onset of co-occurrence may disrupt the course of cognitive and emotional development and may negatively impact an individual's life and well-being (i.e., education, work, relationships, health, and safety). Due to the lack of appropriate and integrated healthcare services for co-occurring disorders, affected individuals are more likely to experience negative outcomes and become high-end users of healthcare resources (3). Thus, investigative efforts (including the present thesis) in this important topic are needed.

4.2 First study (Chapter 2): Purpose, key findings, recommendations, and future research

4.2.1 Purpose

The purpose of the first study was to determine and quantify the association and directionality between mental health disorders (depression and anxiety) and substance use (alcohol, cannabis, and tobacco) among adolescents and/or young adults by conducting a systematic review and meta-analysis. This is an important and growing public health concern that has been widely published in the literature. However, to date, our understanding is limited and the reported findings, at times have been conflicting. To address this issue, a systematic review (the collection and synthesis of all relevant and empirical evidence) and meta-analysis (statistical analysis summary) was conducted. Our study supports the premise that evidence-based, decision-making is integral for the development, evaluation and implementation of interventions that address mental health disorders and substance use among adolescents and young adults.

4.2.2 Key findings

Our systematic review and meta-analysis, included 36 (19 cross-sectional and 17 longitudinal) studies. We found a significant positive association between: 1) depression and alcohol use (OR=1.50, 95% CI: 1.24-1.83); 2) depression and cannabis use (OR=1.29, 95% CI: 1.10-1.51); 3) depression and tobacco use (OR=1.65, 95% CI: 1.43-1.92); 4) anxiety and alcohol use (OR=1.54, 95% CI: 1.19-2.00); 5) anxiety and cannabis use (OR=1.36, 95% CI: 1.02-1.81), and 6) anxiety and tobacco use (OR=2.21, 95% CI: 1.54-3.17).

Further analysis showed a significant positive bidirectional association between tobacco use at baseline leading to depression at follow-up (OR=1.87, CI=1.23-2.85) and depression at baseline which lead to tobacco use later in life (OR=1.22, CI=1.09-1.37). Additionally, we found a significant unidirectional relationship between cannabis use at baseline leading to depression at follow-up (OR=1.33, CI=1.19-1.49).

4.2.3 Recommendations

In our study, the co-occurrence of mental health disorders and substance use among adolescents and young adults was significant, and the following recommendations are provided based on our findings.

1) <u>Bilateral cooperation between two nations (U.S. and Canada)</u>

This systematic review focused on mental health disorders and substance use in the U.S. and Canada. These two countries share many common socio-cultural factors, demonstrate similar patterns in the prevalence of mental health disorders and substance use, and report common health priorities (i.e., advancement of mental health and substance use services). However, despite their many similarities, they also present distinct differences. For instance, Canadian students reported a lower prevalence of depression and anxiety, while U.S. students had a lower prevalence of substance use (4, 5). Interestingly, a higher proportion of Canadian students reported receiving health-related information about depression and anxiety, while a higher proportion of U.S. students received information about substance use (4, 5). These findings may suggest that awareness campaigns were more effective for mental health disorders in Canada,

and substance use in the U.S. Therefore, it would be advisable for key stakeholders at educational settings in both the U.S. and Canada to collaborate and exchange information and ideas on how to further improve their health education and promotion programs. Establishing binational partnerships and cooperation may produce best practice guidelines and effective strategies and interventions for mental health disorders and substance use across campuses in both the U.S. and Canada.

2) Implementation of the quadrants of care model (The New York Model)

In our systematic review, we found significant associations between 1) depression/anxiety symptoms and low intensity of substance use; 2) depression/anxiety symptoms and high intensity of substance use; 3) depression/anxiety disorders and low intensity of substance use; and 4) depression/anxiety disorders and high intensity of substance use. It became apparent that as the severity of mental health disorders and the intensity of substance use varied, different approaches to their healthcare management were needed. Thus, we propose using the quadrants of care model (6), to most appropriately direct the management efforts of the healthcare professional in addressing these two conditions (Table 4.1).

- Depression/anxiety symptoms and low intensity of substance use: individuals treated at primary care settings or referred to other providers with minimal follow-up.
- Depression/anxiety symptoms and high intensity of substance use or depression/anxiety disorders and low intensity of substance use: individuals treated collaboratively by two or more service providers by using referrals with each provider in charge of treating a specific condition.
- Depression/anxiety disorders and high intensity of substance use: individuals treated simultaneously by two or more expert service providers at one point of access to deliver an integrated treatment plan for both conditions.

By following this model, individuals will receive an appropriate level of care based on their needs, and this will ensure efficient use of available resources.

3) Reforming the healthcare system

To address the growing prevalence of co-occurrence of disease (including mental health disorders and substance use), it is recommended that serious consideration is given to reforming

the healthcare system. Healthcare reforms are needed to make necessary changes from the current parallel and independent practice sectors towards coordinated systems of care. To improve efficiency, coordinated practice sectors will require shared funding, developing mandates in concert, and treating affected individuals collaboratively. Reforms should be broad and encompassing all levels of service delivery including health promotion and prevention, diagnosis, treatment, and research.

4) Efficient use of limited resources

Preventive interventions, early detection, diagnosis, and treatment of the co-occurrence of mental health disorders and substance use, can improve the quality of life of adolescents and young adults. Addressing this issue upstream will reduce the associated healthcare costs and permit the efficient use of limited resources, including the need for frequent psychiatric hospitalizations, over-use of emergency departments, and ambulatory care.

4.2.4 Future research

The following three ideas are presented as possible future studies in the examination of mental health disorders and substance use.

1) To examine best practices in the prevention, diagnosis, treatment, and recurrence of mental health disorders and substance use.
2) To determine whether substance use cessation leads to remission of depression or anxiety or treatment of depression or anxiety leads to substance use cessation.
3) To use standardized definitions and categorizations of mental health disorders and substance use along with highly reliable and validated survey instruments to improve comparability between studies.

4.3 Second study (Chapter 3): Purpose, key findings, recommendations, and future research

4.3.1 Purpose

The purpose of the second study was to determine the prevalence and association between mental health disorders (depression and anxiety) and substance use (alcohol, cannabis, and tobacco) among students attending Canadian post-secondary institutions. Despite the high prevalence of mental health disorders and substance use among post-secondary students, little is known about the independent association between these two conditions in Canada. To address this issue, secondary data analysis was conducted. Descriptive statistics of the study population were provided, and multivariate logistic regression models were used to estimate the association between the dependent variables (depression and anxiety) and the independent variables (alcohol, cannabis, and tobacco).

4.3.2 Key findings

Our secondary data analysis was based on the spring 2016 ACHA-NCHA II - Canadian Reference Group survey. Our study found that 14.7% of post-secondary students were diagnosed or treated for depression and 18.4% for anxiety within the past 12-months.

Further analysis showed that the odds of having depression were greater for current tobacco users (OR=1.36, 95% CI: 1.22-1.52) and former tobacco users (OR=1.20, 95% CI: 1.09-1.33). Current cannabis users with (OR=1.17, 95% CI: 1.05-1.31) or without (OR=1.29, 95% CI: 1.05-1.57) other mental health disorders were more likely to have depression. Also, former cannabis users without other mental health disorders were more likely to have depression (OR=1.38, 95% CI: 1.16-1.65). The odds of having anxiety were greater for current (OR=1.41, 95% CI: 1.24-1.62) and former (OR=1.43, 95% CI: 1.22-1.68) female alcohol users.

4.3.3 Recommendations

In our study, the co-occurrence of mental health disorders and substance use among Canadian post-secondary students was significant, and the following recommendations are provided based on our findings.

1) Integrated holistic approach

Mental health disorders and substance use are priority issues in Canada. Therefore, developing a holistic and integrative approach to address these two conditions is critical. Effective leadership and collaborative efforts among key stakeholders (including federal and provincial governments), providers (including community and school-based settings, mental health and substance use clinicians, psychiatrists, and psychologists), and families (living with affected or at risk individuals) are essential to improve healthcare outcomes. Additional improvements to the medical referral system, expanding the scope of provincial healthcare coverage and evaluating existing workforce capacity, training, and flows are paramount.

2) Gender-specific programs

This study found a gender-specific association between mental health disorders (anxiety) and substance use (alcohol) among females. To improve mental health disorders and substance use outcomes, interventions should be gender-specific, relatable, and account for the different risk profiles among the genders.

3) Smoke free campuses

Our study found significant associations and directionality between mental health disorders (depression) and substance use (cannabis and tobacco). Therefore, we strongly support moving to smoke-free campuses. Policies that support smoke free campuses not only provide protection from second-hand smoke, but will help discourage cannabis and tobacco use among post-secondary students.

4) Awareness programs

There are several national awareness campaigns in Canada, addressing the stigma associated with mental health disorders (such as Bell “let’s talk” campaign) (7, 8). However, there is a need for awareness campaigns that acknowledge a link between mental health disorders and/or substance use problems. Such collaborative campaigns may prove beneficial by increasing social supports, reducing barriers in accessing treatment services and decreasing social stigma and discrimination.

5) Training of healthcare providers

It is essential to cross-train healthcare providers from different sectors to increase their awareness of the existing association between mental health disorders and substance use (current and former). There is a need for the characterization of patient risk profiles, the use of valid assessment tools, and updated diagnostic and treatment guidelines to help improve outcomes for these two conditions among adolescents and young adults.

4.3.4 Future research

The following four ideas are presented as possible future studies in the examination of mental health disorders and substance use.

1) To determine the extent of the severity of depression or anxiety associated with the pattern, intensity, and quantity of substance use.
2) To examine documented diagnoses of depression or anxiety from medical records with biologically quantifiable substance use.
3) To assess the sequence of events, relatedness, and temporality between mental health disorders and substance use by conducting longitudinal studies.
4) To determine whether the risk of mental health disorders among former substance users decreases over time.

4.4 Conclusion

Mental health disorders and substance use are interlinked and represent a serious threat to the health and well-being of adolescents and young adults. The co-occurrence of these two

conditions presents complex challenges in their prevention, diagnosis, and treatment. If left untreated, these conditions may result in loss of productivity, poor educational outcomes, increased psychiatric hospitalizations/emergency department visits, inefficient use of limited healthcare resources, and a higher prevalence of chronic diseases. By affecting change at the personal (increase awareness), interpersonal (decrease stigma), and societal (policies and interventions) levels, we can assist adolescents and young adults to make better choices, seek supports as needed, and live healthier and well-adjusted lives.

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Table 4.1: Quadrants of care model

		Intensity of substance use	
		Low	High
Severity of depression/anxiety	Symptoms	Individuals treated at primary care settings or referred to other providers with minimal follow-up	Individuals treated collaboratively by two or more service providers by using referrals with each provider in charge of treating a specific condition
	Disorders	Individuals treated collaboratively by two or more service providers by using referrals with each provider in charge of treating a specific condition	Individuals treated simultaneously by two or more expert service providers at one point of access to deliver an integrated treatment plan for both conditions